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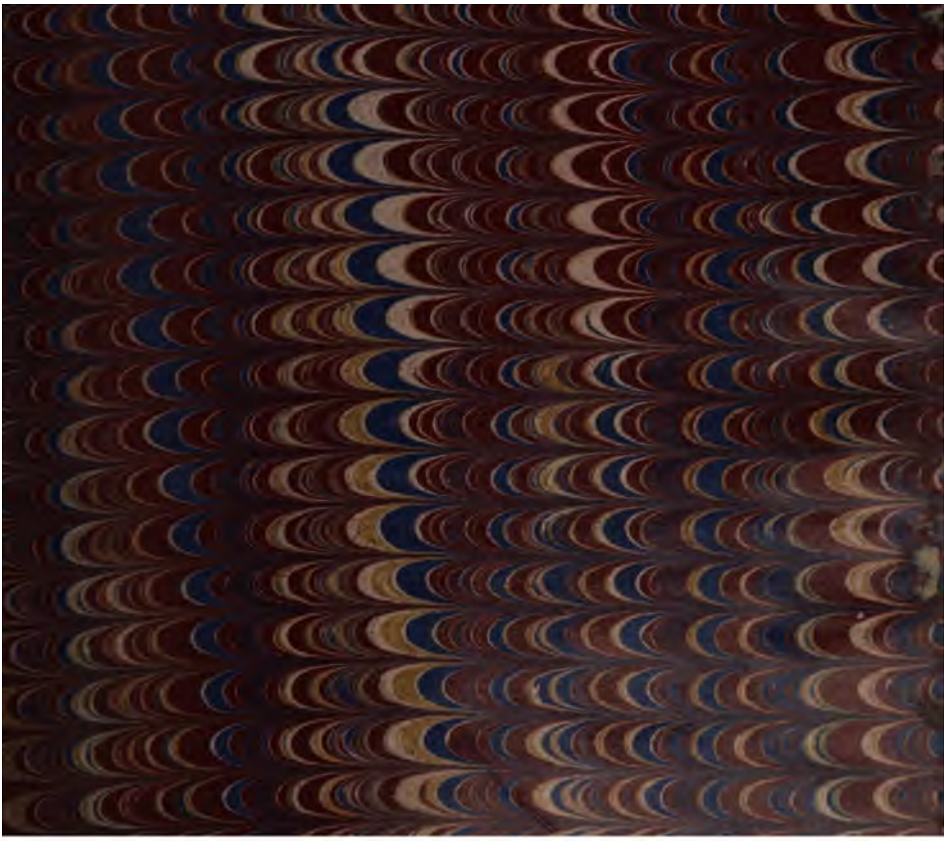

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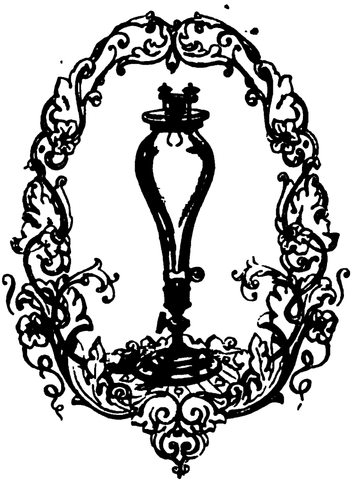

FOUNDED 1846.

PHYSIOLOGICAL CHEMISTRY.

BY

PROFESSOR C. G. LEHMANN.

VOL. I.

TRANSLATED FROM THE SECOND EDITION

BY

GEORGE E. DAY, M.D., F.R.S.,

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS, AND PROFESSOR OF MEDICINE IN THE UNIVERSITY OF ST. ANDREWS.

LONDON:
PRINTED FOR THE CAVENDISH SOCIETY,
BY
HARRISON AND SON, ST. MARTIN'S LANE.
MDCCCLI.

TRANSLATOR'S PREFACE.

In presenting Lehmann's "Physiological Chemistry" to the Members of the Cavendish Society, I feel that it would be superfluous to offer any remarks on the author's high reputation as a general cultivator of chemical science; to recapitulate his numerous and important contributions to physiological chemistry; or to refer to the very favourable reception which this work has received in Germany.

The first edition of this volume appeared in 1841, and the second (from which this translation is executed) in the beginning of last year.[*] If, during that interval, the progress of physiological chemistry has been so rapid as to necessitate the entire remodelling of the work (see p. vii), the shorter period that has elapsed since the appearance of the second edition has been proportionally fruitful in important discoveries. Need I advert to the detection of succinic acid as a morbid product in the human organism, to the later researches of Schwartz on hippuric acid and the hippurates, to the detection of hippuric acid in the blood of the ox, and of oxalic acid in diseased human blood, to the discovery of hypoxanthine and inosite, or to Liebig's important memoir on the fibrin of muscular fibre?

As Professor Lehmann will probably append a supplement to his third and concluding volume, so as to embrace a notice of the discoveries which have been made during the progress of publication, I have abstained from anything beyond the very briefest enunciation of any of these recently discovered facts, and have frequently contented myself with a mere reference to the original source of information.

I have deemed it advisable not to interfere with the thermometric scale, weights, and measures, that are now almost universally adopted on the Continent. Degrees of temperature in this work are always expressed in the centigrade scale, but at page xii, the reader will find a table by which he can, at a glance, discover the degrees, according to Fahrenheit, corresponding with every temperature referred to in this volume. The gramme has now become a recognised standard weight in all our laboratories; in all the cases where it occurs in this work, sufficient accuracy will be attained if we regard it as equal to fifteen grains and a half.

---

[*] Lehrbuch der physiologischen Chemie. Von Prof. Dr. C. G. Lehmann. Erster Band. Zweite gänzlich neu umgearbeitete Auflage. Leipzig, Verlag von Wilhelm Engelmann. 1850.

The author, in his foot-notes, very commonly refers to German translations or abstracts of French and English Memoirs; in almost every case I have given the corresponding reference to the original source. His numerous references to Dr. Golding Bird's researches are made to Eckstein's translation of a Course of Lectures by that gentleman, which appeared nine years ago in the "Medical Gazette," and I have deemed it expedient slightly to modify a few sentences in the text, which express views somewhat different from those given in the third edition of the "Urinary Deposits."

If, in a few cases, I have ventured to deviate from the ordinary nomenclature,* I have not done so without due consideration, and without the sanction of the most competent judges.

I cannot allow these pages to leave my hands without expressing my general obligation to the Council of the Cavendish Society for the readiness with which they accepted my suggestion, that a translation of Lehmann's "Physiological Chemistry" should appear under their auspices, and for entrusting me with the office of Editor. To Professor Graham, Dr. Hofmann, Mr. Redwood, and Dr. Pereira, I am specially indebted, for much kind aid and many valuable suggestions.

G. E. D.

ST. ANDREWS,
July 9th, 1851.

---

* I have, as a general rule, adopted the final syllable *ine*, both for the true alkaloids, and for those allied substances which are described in the same section, but do not present any very distinct basic characters, as, for example, *creatine*, *allantoine*, and *cystine*. The terminal *in* refers to neutral bodies, as, for instance, *asparagin*. I have felt considerable difficulty in the nomenclature of the acids: most commonly I have converted the German antepenultimate *in* into *ic*; thus, *Inosinsäure* is translated *inosic acid* (except by inadvertence in p. 50), *Vaccinsäure*, - *acid*, &c.

AUTHOR'S PREFACE.

SINCE the publication of the first edition of this work, Chemistry—and more especially Physiological Chemistry—has been so zealously and extensively cultivated, and has been enriched by the acquisition of so large a mass of new facts and discoveries, that we may regard the last ten years as one of the most important periods in the history of this science. Hence a simple enlargement of the earlier edition would not have enabled us to consider all the advances made within this short period, which rather required that the whole work should be entirely remodelled, both in relation to its form and contents. The most superficial comparison of the two editions will suffice to show that this volume has been subjected to so entirely new a mode of arrangement, that only a few paragraphs have been borrowed from the earlier edition; for thus alone could a faithful representation of the present state of this department of chemistry be afforded.

The rapid advance of science and the extraordinary accumulation of a mass of crude materials, some of which may not even be capable of acquiring form, must plead in extenuation of the delay that has attended the publication of the second volume. There are, however, two causes which render this delay in some degree pardonable. The one depends upon the intimate connexion of the objects under consideration with histology, the history of development, and pathological anatomy; and as the censure, which has more or less justly been thrown on the writers on physiological chemistry, may be traced to ignorance or neglect of the kindred branches of science, the author has endeavoured to fit himself for the task of critically reviewing the labours of others, by acquainting himself, through personal observation and experience, with the grounds on which these departments of science are based. The great mass of voluminous and often obscure materials presented by physiological and pathological histology must necessarily be subjected to a critical examination before they can be incorporated with physiological chemistry, and hence the author regards such a course of self-training as indispensable in the attempt to furnish his readers with a systematic arrangement of facts. Moreover, those departments of science which must serve as a basis to physiological chemistry, have been encumbered with an accumulated mass of observations, from which have arisen numerous hypotheses successively displaced by others not unfrequently of an opposite character. We must, therefore, as far as is possible, attempt to judge for ourselves if we would not be continually drawn aside by the opinions which are ever rising and falling amid the fluctuations of ephemeral literature.

But the most important reason for the delay that has occurred in the publication of the second volume is, that in Physiological Chemistry, even more than in Zoo-Chemistry, we are obliged to depart from the sure ground of exact enquiry, and to proceed to the consideration of chemico-vital processes, which lie beyond the scope of direct observation, and are thus called upon to admit the correctness of deductions, whose logical authority is not always easy of recognition. Modern science has directed its highest energies to this point of physiologico-chemical investigation; and it was therefore to be expected that this yet imperfectly cultivated soil would give birth to a number of more or less ingenious hypotheses, which can only be sifted by independent examination and positive investigations. But since even this protracted delay and the frequent reconsideration of all the materials at his command, do not give as satisfactory a result as the author could wish, he has at length determined to send forth this attempt at a History of Physiological Chemistry, trusting to the indulgence of those who are labouring in the same cause.

LEIPSIC,
September, 1849.

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TABLE OF THERMOMETRIC DEGREES.

C.	F.	C.	F.	C.	F.	C.	F.
−123° =	−171°·4	44° =	111°·2	85° =	185°	155° =	11°
− 20	− 4	49	120·2	90	194	157	314·6
− 15	+ 5	50	122	92	197·6	160	320
− 9	15·8	55	131	99	210·2	165	329
− 1	30·2	56	132·8	100	212	170	338
0	32	56·3	133·3	105	221	176	348·8
4	39·2	76·5	133·7	106	222·8	178	352·4
6	42·8	57	134 6	107	224·6	180	356
7	44·6	58	136·4	110	230	182	359·6
10	54·5	60	140	115	239	195	383
14	57·2	61	141·8	116	240·8	200	392
15	59	62	143·6	117·3	243·1	202	395·6
16	60·8	63	145·4	118·5	245·3	205	401
17·5	63·5	64	147·2	120	248	210	410
20	68	65	149	125	257	215	419
25	77	65·5	149·9	127	260·6	220	428
26	78·8	68	154·4	130	266	228	442·4
30	86	70	158	133	271·4	232	449·6
32	89·6	73	163·4	135	275	236	456·8
35	95	75	167	136	276·8	239	462·2
36	96·8	76	168·8	137	278·6	240	464
37	98·6	78	172·4	140	284	250	482
38	100·4	79	174·2	145	116	255	491
40	104	80	176	150	302	300	572
42	107·6	83	181·4	152	305·6	360	680

ERRATA.

Page 5, line 9 from bottom, *for* "causal" *read* "casual."
Page 32, „ 3 „ „ *for* "formiate" *read* "formate."
Page 39, last line, *for* "conjugate" *read* "adjunct."
Page 50, line 10 from top, *for* "inosinic" *read* "inosic."
Page 52, line 10 from bottom, *for* "ferricyanide" *read* "ferridcyanide."
Page 81, line 3 from top, *for* "benzoyle" *read* "benzoyl."
Page 81, line 18 from bottom *for* "throughout" *read* "through it."
Page 97, line 12 from top, *for* "and" *read* "under."
Page 139, line 19 from bottom, *for* "creatine" *read* "creatine as."

METHODOLOGICAL INTRODUCTION.

THE application of Chemistry to the elucidation of physiological and pathological processes has been so universally admitted during the last ten years, that it would appear almost superfluous to commence this work with any observations on the importance of this science. While at no very remote period we had occasion to defend this recent department of chemical science from the attacks and unfavourable criticisms called forth by its injudicious application, and by the numerous misconceptions which characterized its early development, we are now almost constrained to withhold from it the confidence which has been too liberally awarded it. Enthusiasm in the cause of organic chemistry has degenerated amongst many physiologists and physicians into a fanaticism, which, even in the best cause, tends to invalidate a host of truths in its endeavours to uphold some single fact. We might be disposed to ask, whether its most zealous partisans have not retarded rather than accelerated the period at which it will attain its proper share of appreciation, and its just recognition. In commencing, therefore, the subject of physiological chemistry, nothing is more important than clearly to understand the nature of the results which this department of science is now capable of yielding, and the requirements which, in its present stage of development, it fulfils; and to ascertain the course, the means, and the methods most likely to lead us safely within its domain, and at the same time the best adapted to promote its further progress.

In entering upon this subject, it may not be altogether unprofitable to begin by indicating the numerous errors into which those most zealous in their endeavours to elucidate physiology and medicine, have occasionally been led by chemical theories and enquiries. These errors appear to us to have diverged in three different directions. In the first place, too little attention has been directed to the laws of a true natural philosophy, whose simplest rules have in many cases been wholly disregarded; in the next place, the necessary causal connexion existing between chemistry and physiology, as well as between histology and pathological anatomy, has too often been entirely neglected; and lastly, much misconception has arisen from the assumption that chemistry afforded a satisfactory solution to many questions which it is either wholly incompetent to answer, or which must at all events remain undecided in the present state of our knowledge.

While we still find occasion to deplore the absence of the steady influence of a true natural philosophy in the application of chemistry to the science of general life, we do not refer to any of those nearly exploded systems of natural science which may be regarded almost in the light of poetic fictions, but to that Newtonian method of contemplating nature, which has carried Astronomy to its present high state of perfection, and has led to the most brilliant discoveries in physics. It is this method of viewing nature which Fries alone understood how to raise into a system, and to which the immortal Humboldt has given life and expression in his 'Cosmos.' It is only by the application of abstract physical laws, by the establishment of certain momenta of empirically observed phenomena, and by a steady adherence to safely guiding maxims, —in short, by logical sequence,—that we can advance in the investigation of vital phenomena. It would almost seem as if medicine, in the earlier periods of its history, had cast a shadow over those kindred sciences which are able to afford it aid and support, clouding even their brightest points. It has thus been found impracticable at once to rid medicine, notwithstanding its assumed physiological character, of the mania of attempting to explain everything by the old system of hypotheses; and hence this science has derived less benefit than many others from the exact method of physical enquiry, having simply borrowed certain materials from chemistry and the kindred natural sciences, and substituted, in the place of the older vagaries of natural philosophy, various chemical phrases and high sounding terms, scarcely less devoid of true import than the former. This deficiency in logical sequence, which we so frequently at present encounter in medicine, has unfortunately also infected animal chemistry; for here likewise facts have not been sufficiently distinguished from hypotheses, or hypothesis from fiction. This is more easily accounted for in physiological than in pure general chemistry: for while the latter treats almost exclusively of palpable phenomena and of well-established facts, which easily admit of being reduced to definite laws, in the former we must necessarily have recourse to experiments and natural investigations, whose success must in a great measure depend on individual operations of the mind. Zoo-chemical processes are the most complicated of any comprised in the domain of natural enquiry; but such processes are not capable of tangible demonstration, but must be divined, or rather, intellectually apprehended. Our senses are incapable of perceiving the causal connexion of things, or the logical succession of phenomena; thus we do not see motion, but simply recognize it by the result of the changes effected by it; we do not perceive heat, but simply the variations of the temperature, and the results to which they give rise, &c. Hence it is not our senses which here deceive us, but the judgment which we form regarding the objects presented to us by the perceptive faculties. The causal connexion of several allied phenomena, (*i. e.*, a process,) can therefore only be comprehended by the subjective combination of individual objects perceived by the senses, and not by sensuous intuition alone. But as soon as we subject to investigation the highly complicated chemical phenomena of life, we enter upon the actual domain of hypothesis. It unfortunately happens, however, that the correct logical conception of an hypothesis has been completely lost sight of, and its place supplied by the vaguest fictions; whence the term has fallen into such discredit that many have been desirous of setting aside all hypotheses, unmindful that even the simplest form of experiment cannot be prosecuted without their aid. Hypotheses are indispensable in every physical enquiry, and must constitute the base of every experiment, as they are in fact merely the subjection of our thoughts and mode of intuition to the reality of phenomena. The question, however, always is, whether the facts at our command logically justify such a procedure, since where such is not the case, the deduction at which we arrive is undeserving the name of an hypothesis, and is a mere fiction, supported at best on a hypothetical foundation.

Physiological chemistry has given rise to many delusions of this nature, owing to its imperfect development, and to the necessity presented by physiology and pathology for chemical elucidation. Some few isolated deductions were drawn from superficial chemical experiments, and arranged in a purely imaginary connexion by the aid of chemical symbols and formulæ, for whose establishment analysis in many cases did not even afford any sanction. Thus, for instance, in the attempt to form a conclusion regarding the metamorphosis of the blood from an elementary analysis of its solid residue and of the composition of the individual constituents of the excretions, there is an utter absence of all scientific groundwork; for, independently of the fact that the elementary analysis of so compound a matter as the blood is incapable of yielding any reliable results, and cannot, therefore, justify the adoption of any special chemical formula, it is assuredly most illogical to attempt to compare the composition of the blood collectively, with that of the separate excrementitious matters. In such deductions, expressed by chemical formulæ, the addition of atoms of oxygen, and the subtraction of those of water, carbonic acid, and ammonia are wholly arbitrary: for chemical analyses do not afford the slightest grounds for the majority of these equations. When, on the other hand, we have seen uric acid decomposed by different oxidising agents into urea and other bodies, and when, further, we find the quantity of uric acid increased in the urine in those cases where a diminished quantity of oxygen is proved to be contained in the blood, we are justified in concluding that also in the animal organism a portion, at least, of the urea found in the urine must have been produced by the oxidation of the uric acid. In the formula which expresses this deduction, we have an hypothesis, but a well-grounded one, which, although requiring further confirmation, is yet wholly different from the frequently condemned, but rarely avoided, abuse of chemical symbols. Chemical equations having no other foundation than the presumed infallibility of empirical formulæ, must, however, cause us to deviate from the path of physical enquiry, and involve us in a chaos of the most untenable delusions. Thus, for instance, a chemical equation might lead us to conclude that glycine (glycocoll) was the source of urea and lactic acid in the metamorphosis of the animal tissues; for we might conclude that 2 equivalents of hydrate of glycine were decomposed into the above-named substances according to the formula, $C_8 H_{10} N_2 O_8 = C_2 H_4 N_2 O_2 + C_6 H_5 O_5 . H O$. All experiments hitherto instituted with glycine are, nevertheless, opposed to such a disintegration. If, then, we would deduce urea and lactic acid from glycine, which has not been proved to exist in the blood, we should be neglecting the most comprehensive rule of logic, according to which one hypothesis cannot be supported by another. It has, however, unfortunately been too much the practice in recent times to employ far more complicated equations as supports for such purely subjective modes of contemplation, by which a semblance of the most exact method of investigation has been assumed. By these means a number of chemical fictions have supplanted the fancies of that speculative natural philosophy which in earlier times encumbered the study of physiology and pathology, and have plunged medicine into the midst of a new labyrinth of untenable theories.

We have indicated a further cause of the partial failure of the application of chemistry to vital phenomena, in the imperfect causal connexion among the different branches of natural science, without which there can be no proper insight into the course of different phenomena, or any recognition of the complete vital process. This is especially the case in reference to pathologico-chemical enquiries, in the majority of which the data yielded by pathological anatomy, and the diagnosis thus afforded, have been too little regarded, whilst the adherents of the pathologico-anatomical school have made free use of chemical phrases and fictions, without an adequate acquaintance with the general science of chemistry. If chemical investigations regarding objects belonging to pathological anatomy would aspire to a scientific value, and if they are to afford any true elucidation of pathological processes, it will assuredly be admitted that the question should be adequately considered from an anatomical and diagnostic point of view. Yet every day presents us with instances of the most flagrant neglect of this self-evident proposition. How frequently we hear of the chemical examination of diseased bones without any regard to a diagnosis at all in accordance with the present condition of pathological anatomy! What numerous analyses have been made of the bones in osteomalacia, notwithstanding that the morbid appearances of these bones vary so much as to render a definite diagnosis a matter of extreme difficulty to the pathological anatomist! We even more frequently meet with similar inconsistencies in the investigation of diseased animal fluids. Here, as in the statistical method of observing diseases, none but the simplest form of a disease should be made the subject of such enquiries. Yet the causal results yielded by an examination of the urine and the blood in the most complicated forms of disease, are frequently made the sole grounds for drawing conclusions regarding the morbid process itself. In many cases even the true diagnosis of the disease has not been given. Thus, for instance, we are told that the blood has been analysed in typhoid pneumonia, yet when we read the history of the case, we find that the disease was neither ordinary abdominal typhus with pneumonic exudations, nor what is termed pneumo-typhus, but simple pneumonia with cerebral symptoms.

More frequently still, we are obliged to rest content with vague names of disease, unsupported by any history of the case. In most cases certainly the name of the disease is unimportant. It is by no means essential to the scientific comprehension of such enquiries that the whole history of the case from beginning to end should be given with the circumstantiality at present so much in requisition; but we undoubtedly ought to indicate the condition of the patient, as ascertained by a physical examination, at the period of the removal of any morbid product for chemical investigation. It is the practice in reporting chemical investigations, to detail as minutely as possible the method pursued, that the reader may be able to judge for himself, and test the correctness of each individual step. A similar rule should be observed with reference to the state of the disease in all pathologico-chemical investigations, for it is only by these means that we can impart scientific value to such enquiries. We shall find, however, on examining our pathologico-chemical literature, that this principle is too frequently neglected.

If we would render chemistry truly useful to other departments of natural science, we must be careful to acquire a proper knowledge and a due estimate of the advances made in each; a point which has unfortunately been too much disregarded in reference to histology. We have passed the age when morbid tumours, without regard to their histological constitution, were crushed and pounded in a mortar, with the view of extracting from this artificially produced chaotic mass a principle peculiar to cancer or pus,—a scirrhin or a pyin; but at the present day the combustion tube is still misused in the determination of the elementary composition of a mass made up of the most heterogeneous organic parts. Such analyses are wholly devoid of chemical or physiological value, and cannot, as all chemists must allow, in any way contribute to extend the domain of chemistry, while they are useless alike to the physiologist and the pathologist, being utterly devoid of all scientific links of connexion. If, however, we take physiology for our guide in such researches, we shall find support from that unity of character to which every scientific enquiry, and every successive experiment should be reduced.

Pathological tumours afford a good illustration of the extent to which the success of a chemical investigation, and of the method of analysis, depends on a correct physiological view of the question. When we consider the most recent investigations made in relation to this subject, we are led to regard malignant tumours, not as secondary products or parasitic organs, but as exudations which have been arrested in different stages of development and organisation. If we adhere to this point of view, we shall no longer attempt to discover the special matters of scirrhus, encephaloid, &c., but shall rather look upon these objects as the means of furnishing us with a clue to the physiologico-chemical processes by which the plasma is developed into cells and fibres, which have hitherto presented insuperable obstacles to the advance of chemical enquiry.

In adverting to the false position assumed by pathological chemistry in reference to pathological anatomy, it must not be forgotten that the pathologico-anatomical school is equally deserving of censure. Whence comes it, we may ask, that those who would set aside pathological anatomy, and who profess to limit their investigations to the actual facts of medicine, should threaten us with all the horrors of a transcendental humoral pathology? The solution of this question is to be found in the circumstance that, strictly speaking, pathological anatomy is occupied only with the external palpable alterations experienced by the tissues and juices from the action of disease, and that if any of the more gradual stages of transition be made apparent in the course of such processes, these are mere forms or facts, and afford no insight into the *modus* of the organic changes. In a word, pathological anatomy is a purely descriptive science, a natural history of morbid actions, which may lead to the establishment of a system, but not to that of a general principle and to conclusive deductions. It is the geognosy of the morbid organism, and must be allied to a geology of disease which, however, it is incapable of establishing. It is precisely the purely descriptive character of pathological chemistry that places it beyond the sphere of experiment. Like geognosy, it can only attain its aim—the scientific recognition of objects—with the cooperation of physics and chemistry. If, however, pathological anatomy is to be regarded as the surest foundation of medical science, we must endeavour, on speculative grounds, to ally it more closely with pathology, and thus render it, to a certain extent, more acceptable to the medical public. We are convinced that the principal object had in view by the founder of German pathological anatomy, Rokitansky, in writing the first volume of his celebrated work, which has been so severely criticised, was simply to indicate to pathologists the points of view from which the fruits yielded by the pathological anatomy he had himself established might be most fully comprehended. But it has unfortunately happened that his followers have frequently borrowed from physics and chemistry phrases and modes of representation, without seizing the spirit of these sciences, or even comprehending their methods of operation. Hence there has emanated from this school, notwithstanding the positive observations on which it is based, a multitude of the most unsubstantial medical fictions which, for shallowness, yield to none of the earlier schools. Pathological views in reference to the nervous system (Nervenpathologie) have been elevated to the prejudice of physical views (Nervenphysik); for here, in consequence of ordinary anatomy being inadequate to explain pathological changes, ideas, or rather mere words, have been unscrupulously borrowed from organic chemistry (by those who were perfectly ignorant of this science) to explain the most complicated processes, of which scarcely anything was known but the final results. Some adherents of the pathologico-anatomical school have presented us with a theory of the crases of the blood in different diseases, although this is a view in which no chemist could at present seriously concur. This theory of crases has been so thoroughly investigated by physiologists in recent times, and its want of foundation made so evident, that we need advert no further to it than to observe that where admixtures and separations are concerned, the chemist is the only competent guide.

A third circumstance which has led to misconceptions in physiological chemistry depends upon an over-estimate of the value of chemical auxiliaries, and a complete ignorance of the present condition of organic chemistry. Have the numerous analyses of morbid blood instituted during the last few years fulfilled the expectations of physicians? With all due gratitude to the indefatigable investigators who, with no other aid than that which zoo-chemistry could offer, boldly attempted to throw light on those obscure enquiries, it must be admitted that, when we seriously enquire into the recompense of all their labours and sacrifices, we find that the result, although too dearly bought, was altogether inadequate to satisfy the requirements of pathology. Have the numerous analyses of the urine led to much more than the assumption of several new species of disease, or so-called diatheses? Although we might have anticipated greater results, we can hardly wonder that the efforts hitherto made should either wholly or partially have deceived our expectations; for although these investigations may have rendered chemistry no unworthy auxiliary to a physical diagnosis, analyses of morbid products could hardly afford an insight into the chemical laboratory of the organism, while the means were wanting to prosecute them with the scientific accuracy attainable in the case of mineral analyses. Animal chemistry is still wholly unable to afford us a precise, and at the same time a practically useful method of investigating the blood; and how should it be otherwise while we continue to be in doubt regarding the chemical nature of its ordinary constituents? The mineral substances of normal blood are not yet determined, or, at all events, continue to be made the subject of dispute; we scarcely know the names of the fatty matters it contains; one of its most important constituents, fibrin, cannot be chemically exhibited in a pure state; we are ignorant of the nature and mode of secretion of the globulin of the blood-corpuscles; we are still far from being able to separate and determine the so-called protein oxides; and we are also ignorant of the excrementitious substances occurring in the blood. How then, amidst these and a thousand other uncertainties and doubts, can an investigation of the blood be scientifically and trustworthily conducted? We analyse healthy and morbid milk, and yet we are ignorant of the substances whose admixture we have termed casein. The urine, in its morbid condition, presents many varieties; and yet our knowledge of this secretion, frequently as it has been analysed, amounts to little more than an acquaintance with the quantitative relations of some of its principal constituents; creatinine and hippuric acid have not been determined by any analysis, and doubts are still entertained by some chemists, (although most unjustly,) regarding the presence of the latter in human urine, while absolutely nothing is known regarding the most important pigment of this secretion. Many experiments have been made and theories broached on nutrition and digestion, and yet to almost the present day the existence of lactic acid in the gastric juice has been contested. Although hypotheses are not wanting regarding the mode of action of pepsin, we know nothing of its chemical nature, and we are wholly ignorant of the proximate metamorphosis of albuminous bodies in the stomach during the process of digestion. Will Mulder be able, even with his most accurate analyses, to support his protein theory by the aid of sulphamide and phosphamide? or is this term destined merely to indicate a past epoch of organic chemistry? When such is the state of animal chemistry, can we wonder that there should be obscurity regarding the chemical processes in the animal body, their various isolated and combined actions, their causal connexion and their dependence on external influences and internal conditions? Unfortunately, we might be led to believe, from the lectures and writings of many physicians, that, trusting to the aphoristic and often highly apodictic assertions of certain chemists, they felt secure of having reached the object of their enquiries. Although at present little more than the direction is indicated, we may hope in due time, and after innumerable efforts, to see our endeavours crowned with success.

After having become acquainted with the deficiencies and errors belonging to the chemistry of the vital processes, which was so prominently brought forward at an earlier era, we will now pass to the methods and principles by which alone this science can be made to fulfil its just requirements. The final result of all physiologico-chemical investigations is avowedly that of gaining an accurate knowledge of the progress and causal connexion of the chemical phenomena attending the vital processes. To attain to this knowledge, it is not sufficient to detach separate parts from the mechanism of the whole, and to form an opinion of the combined action of so complicated a chemical structure from a more or less superficial examination. Attempts have already been made to establish a splendid theory of the metamorphosis of tissues, but notwithstanding the many able heads and hands that have been engaged in the labour, it is still deficient in the essential of a solid foundation.

It is unnecessary to prove that we must thoroughly understand the substrata of the metamorphosis of the animal tissues before we can venture an opinion on the nature of the processes. The surest supports of physiological chemistry are to be sought, therefore, in general organic chemistry; while the study of the organic substrata of the animal body, or zoo-chemistry considered in the strict sense of the word, must necessarily constitute an integral part of physiological chemistry and prove a most efficient aid towards its development. If zoo-chemistry ever fulfil its object, it must be by the joint aid of chemistry and physiology; that is to say, individual substances must not only be fully examined in reference to their chemical value and their place in the domain of pure organic chemistry, but they must also be observed in the more general relations which each may bear to the animal organism and its metamorphosis. In a word, the physiological value of each substance should be as carefully considered in zoo-chemistry (the basis of physiological chemistry) as in pure chemistry. It seems to us, that in treating of zoo-chemistry (in the first volume of this work,) we shall the best attain this aim by adopting the following arrangement:—namely, by treating of the *chemical* relations of each body in reference to its properties, composition, combinations, and mode of decomposition, its preparation, the method of testing for it, and its quantitative determination; in explaining the *physiological* relations of each substance, we shall endeavour to determine its occurrence in the animal body, and its origin, (whether it be produced within or without the body,) and from the above considerations, we shall finally attempt to deduce its physiological value.

We shall treat of the properties of each organic substratum before considering the remaining chemical relations, as it appears to us both unpractical and illogical to begin with the mode of preparation, as is usually done; unpractical, because no student can comprehend the mode of preparation when he is not in some degree acquainted with the properties of the substance in question, and illogical, because we must have some idea of a body before we can attempt to prepare or exhibit it. The composition of a body must necessarily constitute the most important subject of consideration after its properties and its principal reactions have been duly noticed, for it is only by such means that we can attain to an idea of the nature of a substance, and of the place it occupies in the system of organic chemistry. Hence this section must not be limited to a mere enumeration of analyses or of empirical formulæ, but must embrace a consideration of the arguments that are adducible in favour of the different views of the theoretical internal constitution of a substance, and which are briefly expressed by the rational formulæ. This method is of the greatest importance for the recognition of the physiological relations of organic substances; since without it, we are unable to arrive at any logically correct judgment regarding the origin and the physiological importance of different substances. If a knowledge of the composition of an organic substance were not necessary to the investigation of its *combinations* and *products of decomposition*, we should have placed it after the latter, since they constitute the safest grounds from which we may form an opinion of the rational composition of a body. A careful study of the products of decomposition is however the more necessary, since it is mainly on these that we must base our view of the metamorphoses experienced by any given substance within the vital sphere.

It is only when all these relations have been considered, that we shall deem it expedient to enter upon the different methods of preparation or exhibition, for then only can the directions given for the separation of substances be understood.

Before considering a substance from a physiological point of view, we must examine the means by which we are best able to demonstrate its presence in the animal juices and tissues. The qualitative analysis of organic bodies is still far behind that of inorganic bodies, but attention to this point is the more necessary, since deficient investigations too often lead to hasty and erroneous opinions. Nor does less importance attach to a correct estimate of the methods that have been employed for the quantitative determination of the main constituents of animal fluids; for it is only by this means that we can form an opinion of the value of many of the existing quantitative analyses of physiological and pathological products, and of the conclusions which we are justified in deducing from them.

The physiological consideration of every substance must of necessity be primarily based on its mode of occurrence, for we cannot form any opinion of the importance of a body in reference to the changes of animal matter without knowing where, in what relations, and in what quantity it occurs. When, however, we have examined the origin and decomposition of a substance, we have obtained the firmest base for the explanation of the vital chemical processes.

After having, in this manner, familiarised ourselves with the organic substrata of the animal body, we are still only on the threshold of the study of the constitution and functions of the animal juices and tissues. Before, therefore, we proceed to the actual study of physiological chemistry, (namely, the theory of the metamorphosis of matter, or of the zoo-chemical processes,) we take into consideration the substances with which we have already become acquainted in zoo-chemistry, regarding them topographically, in reference to their simultaneous occurence, and their blending and admixture under the form of animal juices, tissues, and organs. We may extend this classification to the animal fluids as well as to the tissues and entire organs. No one will deny that the knowledge of the chemical constitution of these more complex and frequently variable parts of the animal body is another basis of physiological chemistry, for it is evident that if we would treat of chemical processes, we ought to have a knowledge of the substances implicated in them. This however, cannot yet be attained in zoo-chemistry in the sense that we attach to this science. We here enter the domain of physiology, in as far as we submit the direct results of physiological actions to an investigation, which however must still be of a purely chemical and essentially analytical character.

The province of chemistry in the consideration of the animal fluids and tissues, is similar to that of mineralogical chemistry, for as in the one case, we seek for elucidation respecting the proximate constituents of often highly complicated compound minerals and rocks, so in the other we endeavour analytically to determine the constitution of animal fluids and solid organised parts by the aid of the knowledge we have already obtained from zoo-chemistry. It was in these data that the nature of physiological and pathological chemistry was formerly studied, and it was believed that the processes themselves might be determined directly from the knowledge afforded by such analyses. The fallacy of such a view is proved no less by the state of our knowledge, some ten years since, regarding the physiology of nutrition and secretion, than by the numerous errors propagated since that period in reference to the chemical processes in the animal body. What were analyses of the blood, urine, milk, and bile before this epoch, but mere isolated facts deficient in those links that ought to bind them to the theory of nutrition and secretion? Physiology then regarded such analyses more as mere accessories than as necessary means for the comprehension of each process. A more exact, although by no means a perfect knowledge of the chemical qualities of these juices was subsequently acquired, and hence it was attempted to establish a more intimate relation between the chemical constitution and the physiological function; but from the absence of a proper analytical foundation, this method not unfrequently led to numerous perversions and dangerous errors, as we have already stated, and as we might illustrate by a large number of examples. Although the results of the chemical analysis of the animal juices may afford many indications of the processes, they by no means enable us to judge of the function itself, however numerous and complete they may be; and it is only by means of experiments founded on the composition of these fluids that we are able to arrive at any satisfactory conclusion regarding the nature of the processes in question.

The study of the zoo-chemical processes based on zoo-chemistry and the theory of the animal juices, appertains to the third section of physiological chemistry, the theory of the metamorphosis of tissues—of nutrition and secretion. It has already been observed, that the actual object of physiological chemistry is to examine the course of the chemical phenomena of the animal organism in their causal connexion, and to deduce them from known physical and chemical laws; or in other words, to explain them scientifically. Even if we regard the chemical substratum, as made known to us by zoo-chemistry and the theory of the juices, in the light of a satisfactorily investigated question, there are still several directions to be pursued before we can reach the proper object of our enquiries. It is here most essential that we should be well acquainted with the paths to be followed, for in our search after truth we are compelled to call to our aid hypotheses which might easily lead us into the domain of pure fiction.

As long as zoo-chemistry and the theory of the juices continue to occupy their present subordinate position, the only method by which the foundation necessary to an exact investigation can be obtained, is that which we may term the statistical. Liebig, Boussingault, and Valentin have indeed, with a more correct view of what was required, attempted to compare the final effects of the whole with the material substrata supplied to the organism. We cannot, it is true, arrive at any conclusion regarding the working of the process itself by a mere juxtaposition and quantitative comparison of the ingesta and excreta of the animal organism, any more than we can judge of the causes and course of diseases by the number of fatal cases recorded: but such experiments furnish us with certain general results which serve as guides to further investigations. Some of the most important questions, whose solution was specially necessary, were unanswerable by any other method. Thus, for instance, it was ascertained, by an accurate investigation of the food, and its comparison with the constituents of the excreta and of the nutrient fluids, that in the ordinary food of animals, albuminous substances occur in sufficient quantity to compensate for the nitrogenous matters lost in the process of nutrition and in the metamorphosis of tissue; while it was thus at the same time shown, that the animal organism does not necessarily possess the property of generating albuminous matter from other substances containing nitrogen. The question whether the animal organism possessed the property of generating fat was answered in a similar manner; and it is well known that by means of such statistical observations, (comparing the fat contained in the food with that secreted in the cellular tissue and mixed with the excrements) the contest carried on between Liebig on the one side, and Dumas and Boussingault on the other, regarding the formation of fat, was finally decided in favour of the former.

This statistical method preserves us from setting up untenable hypotheses, and prosecuting useless experiments. How long were the minds of natural philosophers haunted with the illusion that animal bodies possessed the power of generating mineral elements, as lime, iron, sulphur, &c., from other elements, or even from nothing! It was this method alone which exposed the perfect nullity of the obstinately defended dogma of the 'vital force.'

Statistico-chemical investigations may serve as checks to, or confirmations of other enquiries and methods of enquiry; thus, for instance, Boussingault, by a comparison of the amount of nitrogen in the excrements with that in the food, has fully confirmed the experiments made by Dulong, Valentin, Marchand, and others, which appeared to show that the animal body lost a slight quantity of nitrogen by exhalation from the lungs.

The statistical method would, therefore, appear to be one of the most important aids towards a solution of some of the more general questions in reference to the metamorphosis of the animal tissues. We must, however, be careful not to deduce more from such experiments than what is permitted by the simplest induction; for the results derived from this method have unfortunately too often been made to yield support to the vaguest fictions and the boldest speculations.

It need scarcely be observed that science should not rest satisfied with a knowledge of the final results of chemical processes in the animal body, or with the assertion of the chemical dignity of the vital process *in summâ*, but should be made to enter more deeply into the course of the separate processes, and into the causal relations of phenomena. Here the statistical method cannot of course afford any satisfactory solution to our enquiries; for when we have ascertained by this experimental method that fat is formed in the animal body, we must learn from other methods the manner in which this substance is formed.

The method by which we may examine the course of phenomena and the cause of their succession, might be named *comparative analytical* or *chemico-experimental*, in as far as the chemical phenomena of the living body may be artificially imitated, and the chemical metamorphoses of certain substances external to the vital sphere be compared with those within the influence of the vital processes. Liebig and his school have here done essential service. He was led to believe from his statistical enquiries on fats, that these substances in their transmission through the organism, were in a great measure oxidised and reduced to water and carbonic acid, by which means they specially contributed towards the maintenance of animal heat. As Liebig was by no means inclined to believe, as some have supposed, that fat was consumed in the lungs, somewhat in the same manner as oil burns in a lamp, it was necessary more accurately to investigate its gradual metamorphosis, and its transition through different stages of oxidation, and into bodies containing a larger quantity of oxygen. He believed that he could most readily attain this object by the comparative analytical method; and hence he and his school entered upon a series of experiments on the numerous products of decomposition of fatty matters, and more especially on their products of oxidation; and although we may still be far removed from the object in view, these enquiries have enriched us with many valuable results. A similar instance is afforded by the gelatigenous tissues of the animal body; for although our histological and statistico-chemical investigations leave not the slightest doubt that the gelatin is formed from the albuminous matters, the process of this metamorphosis is still wholly unexplained; and before we shall be justified in forming an opinion regarding this metamorphosis, and expressing it by a chemical equation, it is indispensably necessary that we should investigate the metamorphoses experienced by albuminous bodies during their gradual oxidation. We are indebted for these views to the admirable investigations prosecuted under Liebig's direction, by Schlieper and Guckelberger, on the products of oxidation of albuminous bodies and of gelatin.

As we learn more thoroughly to investigate the processes of putrefaction and decomposition, and that of the dry distillation of individual animal substances, and therefore the better to understand their regressive metamorphoses, we may hope by this knowledge to arrive at a deduction, based on some probability, regarding their progressive metamorphoses. Among these probable deductions we may place Dessaigne's discovery of the decomposition of hippuric acid into glycine and benzoic acid, Liebig's investigation of creatin, and his pupils' analyses of glycine (glycocoll), which although they do not yet afford us any perfect elucidation of the metamorphoses of animal matter, nevertheless yield many sure points of support for future enquiries on the vital processes.

A third method, which although frequently employed, has hitherto, from the imperfect state of our knowledge, yielded few reliable results, is the *physiologico-experimental*. By this term we would designate that class of enquiries, in which observations are made in the living organism on the result of certain conditions on the progress of a physiologico-chemical process, and on the different stages of that process. We are aware that we shall never succeed in artificially reproducing all the processes as they occur in the living body, since we are here as little able to call forth the necessary conditions and relations, as in the formation of minerals and rocks. It is, therefore, the more necessary to observe a process, of which we cannot judge by imitation, in its course in the living body, and for this end we must chiefly employ natural physiological means. Among these we may reckon the investigations that have been made in reference to the contents of the stomach during the process of natural digestion, to the chemical change of individual substances in the development of the egg during incubation, and to the dependence of the products of respiration on different external conditions. We may further add those experiments that have been made on the changes of individual substances during their passage through the animal organism, or on the effect of different kinds of food, and the metamorphoses of certain nutrient substances during the process of nutrition. To the same method belong all pathologico-chemical experiments, as for instance, observations on the contents of the intestine after the closure of the common bile duct, and on the blood and other fluids after extirpating or tying the vessels of the kidneys. Chemistry, unfortunately, too often fails us to permit of our deriving from this method all the results which it appears to promise; it must however, ultimately furnish the key-stone to all physiologico-chemical enquiries, which, without its aid, would continue insoluble enigmas, and would admit of hypothetical rather than actual explanation. The theory of the metamorphosis of animal matter, without the support of such a physiologico-experimental foundation, must continue to be attended by no little risk.

In conclusion, we would advance a few remarks on the place which physiological chemistry occupies, or at some future period will occupy, among the auxiliary medical sciences. If the final result of all physiologico-chemical enquiries be that of comprehending the chemical phenomena of animal life in their different phases and in their causal connexions, it is obvious that we must look to this science for a solution of the most important questions of physiology, and of medicine generally. It cannot be denied that most of the phenomena of animal life either consist in or are accompanied by chemical processes; nor can we form an adequate conception of the functions of the nervous system by which sensuous perception and motion are regulated, without the simultaneous existence of chemical actions. For although we are as yet unable to make nervous action fully harmonise with definite physiological laws, or to identify it with certain physical forces or imponderable fluids, all physiological experiments indicate that it is always followed by a chemical reaction, and that the nervous system experiences chemical changes by and through its own activity. It must, indeed, be admitted that any actual proof of such chemical metamorphoses is at present perfectly unattainable, and that our chemical methods would here afford us no higher aid than that which the scalpel yields to the pathological anatomist. But ought we to despair of attaining our object, because we do not as yet clearly perceive the direction we are to follow? Weariness of the senses is the diminished impressibility of the nerves of sense, but its cause cannot reasonably be sought for in any other than a chemical change, experienced by the conducting substance of the nerves. Such a chemical metamorphosis of the nerves of sense from external impressions can no longer greatly excite our astonishment, since we have witnessed the unexpected phenomenon of a picture produced suddenly, and as it were by magic, from the chemical changes effected by the rays of light on an iodised silver plate. Should we not be equally justified in saying that the iodised plate, which after being exposed for a few seconds to a strong light gives only faint and half effaced images, is wearied like the retina, when after repeated and continuous perception of an image, it gives back only the faint outlines of the object? We may rest assured that the nervous system is not exempt from chemical action; and if the nervous system itself must fall within the domain of chemical contemplation, and a chemical expression remains to be found for its action, no less than for that of digestion and for the formation of blood, it is scarcely necessary to offer further proof of the fact that chemistry is destined to play the most important part in physiology and medicine. However much we may endeavour to exclude chemistry from certain physiological investigations, we shall always find that it involuntarily forces itself upon our notice; for without it we shall be unable to find a physiological equation or a philosophical expression for a process. In a scientific point of view chemistry must, therefore, be regarded as an invaluable acquisition to physiology. We have, then, little cause to dread that Cicero's observation "*Suo quisque studio delectatus alterum contemnit*," will be applied to ourselves, when we assert that physiological chemistry is the crowning point of every physiological enquiry.

When we turn to practical physiology, to pathology, and therapeutics, we are again reminded that chemistry is indispensable. Is there a single disease that is not attended by chemical changes? Can we ever hope to comprehend or explain the nature of any process, if we are ignorant of its integral factors? Life cannot exist without chemical movements, disease cannot exist without chemical changes. Thus much in reference to pathology; while in respect to therapeutics, it is almost superfluous to observe that chemistry here also plays the principal part, for where has modern pharmacology sought its chief support, save in chemical processes and principles? And if we have advanced so far towards a clear insight as no longer to ascribe supernatural forces to medicines, but to derive their efficiency specially from chemical properties, then must chemistry be the supporting basis of pharmacology. The physician acts upon the body mostly by the aid of matter, which retains its characteristic powers within no less than without the organism. If then nervous action likewise falls within the sphere of chemical metamorphoses, the *Nervina* (or *Neurotica*) of pharmacologists must primarily at least act chemically on this system.

To those who stand on the grounds of exact investigation, holding fast to the fundamental principle that it is from physical laws alone we must deduce a true explanation, and that by induction only can we investigate the causal connexion of vital phenomena, no further proof need be adduced of the truth of our assertion that physiological chemistry occupies the highest place among the sciences auxiliary to medicine. Even those who deem special forces and special laws necessary to the explanation of vital phenomena must admit that chemical methods are the most important for the investigation of these actions, and for the solution of such questions, if, as indeed cannot be denied, it is only by a thorough investigation of the physical forces acting in the living body that we can become acquainted with a true vital force or vital law. With those who judge of vital forces by subjective feelings, and would stamp nature with the impress of their own ideas, we will not contest the point of view we have adopted; but leave them to regard chemistry, like physics and anatomy, as a mere auxiliary towards an adequate appreciation and contemplation of nature.

It now only remains for us to add a few words on the relation of pathological to physiological chemistry. Neither from a theoretical nor a practical point of view can we concur in the assertion that pathological chemistry is separate and different from physiological chemistry. Experience shows us the impracticability of such a separation, for how much mental energy has been wasted, as it were, in the investigation of unattainable things; and among these we may class pathological chemistry, when not based on physiological principles. It would assuredly be going too far, to assert that the natural enquirer should undertake no experiment that could not afford a definite solution to a well-grounded question; but it must be admitted that there is an almost countless number of pathologico-chemical experiments which have yielded no result, and which obviously could yield none; and indeed it seems scarcely comprehensible that we should attempt to understand that which is abnormal, while we continue ignorant of that which is normal. Before we can institute a comparison between two things, we must be familiarly acquainted with at least one. Here we do not by any means wish to maintain that no pathologico-chemical enquiries should be prosecuted, for this would be as absurd as to withhold our attention from pathology until we supposed ourselves fully enlightened on the subject of physiology. We would, on the contrary, limit our objections to those analyses of pathological products which have no relation to any one leading idea, are devoid of connexion with any scientifically established fact, and do not bear upon general chemical or physiological propositions. Such investigations are so numerous, that our weekly periodicals are seldom without one or more analyses of diabetic urine. These results would, doubtless afford additional proof of the well-established fact that sugar is present in diabetic urine, if we did not feel assured that the diabetes was not diagnosed until the existence of sugar had been demonstrated in the urine. We seldom meet with any observation on the relation existing between the quantity of sugar excreted in a given time, and the quantity of food taken during the same period; while other and similar considerations of equal importance are also usually disregarded.

The severance of pathological from physiological chemistry is even less admissible in a scientific than in a practical point of view. We will not here pass judgment on the obscure abstract idea of disease, but whatever value such a view may have in reference to life and medical practice, and however pathologists may strive artistically to define it, it must continue illogical in reference to theory and science. But whatever view we may here adopt, it must be admitted that pathological and physiological chemistry cannot exist independently,—a view requiring no circumstantial proof. The power and the law remain the same, whether the points of application be more or less remote from the fulcrum of the lever; the result alone is different. Pathologico-chemical phenomena do not originate in the occurrence of new forces or special laws, but merely from the chemical points of application being somewhat different; that is to say, the relations are changed under which the substrata develope their actions of affinity. Pathological phenomena can, therefore, only be recognised when manifested preponderatingly in some one direction, but they of necessity obey one and the same law. As the result of indispensable conditions we cannot then regard them as anomalous or abnormal. If protoxide of iron is no longer precipitable by alkalies when organic acids are present, and if fibrin loses its capacity for coagulating in the presence of certain salts, we no more apply the term *diseased* to these substances than to a clock which stops because the weight has run down. When, in consequence of any influence, the capillaries become dilated, and the blood contained in them stagnates, exudes, or coagulates, we do indeed recognise the occurrence of something singular and not of ordinary occurrence, but nothing independent of a law. The physician may designate inflammatory symptoms as abnormal and morbid, but the philosophical enquirer sees only the necessary result of laws acting under different relations, for he has to deal only with fixed laws and not with rules abounding in exceptions. The chemist is an investigator of nature even when occupied in studying pathological processes, as the physiologist is still engaged in physiology, when turning his attention to the less frequent phenomena of the living body, for there is no special science for the exceptional phenomena of nature but only one physiology as there is one all-powerful law of nature.

We are tempted, notwithstanding the above observations, to cast a glance at the position occupied by physiological chemistry, in relation to what is called metaphysiology. The recent advances of organic chemistry have unfortunately been interwoven with a fantastic physiology, which designates itself as a comparative science. This is not a science comparing together the functions of the organs of different animals, as comparative anatomy compares their structure, but a system founded on abstractions and ideal comparisons; that is to say, on figurative representations of subjective conceptions, in which the results of objective investigation are advanced in defiance of the most contradictory facts. We entertain all due respect for that form of metaphysics which occupies the same rank among the speculative sciences as physiology and chemistry hold among the exact sciences. Metaphysics and physiology resemble two diverging lines which coincide only in their starting-point, and differ so widely at all other points, that they cannot be united unless to the detriment of true science. The physicist has maintained his stand more firmly and securely than the speculative natural philosopher, who never relaxed in his attempts to force his complex ideas, constructed according to a subjective standard, upon the objective experiments of the physicist. On this principle it has been attempted to anticipate intellectually the discoveries and general propositions which the physicist endeavours to attain by practical evidence, and thus science has been confused in a manner that cannot fail to retard its advance. There are now indeed but few remaining followers of the school of speculative natural philosophy, which emanated from the same exaggerated bias of the age, which in poetry gave rise to the romantic school. Men created for themselves an Ideal to which they gave the name of nature.

Although such a system of metaphysics* completely mistakes its province, it is yet essential that "the chemist should raise himself above the vital, no less than the chemical process, in order to compare them both in their principal properties and results, and to represent them in their co-existence, founded as it is in objective processes." This is, however, a point of view from which no mere chemist should observe the phenomena of nature; for no exact investigation is compatible with imaginative speculation, which can exhibit only artificial comparisons and obscure reflections of dimly comprehended physical phenomena. We have not hesitated to avow that we have assumed a thoroughly radical point of view, in reference to specific vital phenomena and vital forces; for we cannot rest satisfied with the mysterious obscurity in which they have been artificially enveloped. With the physicist we would uphold the reality of phenomena, and while we admit that the consciousness of the reality of matter is only the result of an abstraction, we must regard this abstraction, by which we recognise the Immaterial, the Spiritual, and the Force, as originating in reality. We therefore believe, with the diffidence beseeming a genuine student of nature, that it would be wiser and more conducive to the spread of true knowledge, to adhere, in the study of vital processes, to matter, and to the laws by which it is determined, than, following the fictitious abstractions of dynamical processes, to assume that there exists in life a higher power of the spiritual force pervading matter. While, therefore, in opposition to the views of these natural philosophers, we must refer all force to matter, we have no fear of degrading "vital phenomena to mere mechanical, physical, and chemical processes," since our most exalted conception of nature and the sublimest natural philosophy emanate from the very simplicity of physical laws, and the unlimited variety of phenomena to which they give rise.

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* Geubel, Grundzüge der wissenschaftlichen Chemie, Frankf. a. M. 1846, and L. Müller, Berzelius' Ansichten, Breslau, 1846.

We are firmly convinced that even metaphysiology will be unable to deprive physiological chemistry of the consideration due to it among physical studies, in its explanation of vital processes; and we will, therefore, leave it to the poetic and the imaginative to depict the romance of the protecting activity and sturdy contest maintained by the vital force, and of a struggle between different powers,—between the attraction and repulsion of polarities. Does it not need a superabundant richness of fancy to believe with metaphysiologists, that apparent death, trance, or (as it has been termed) latent life, is the predominance of the spiritual over the material (the metamorphosis of matter being at its minimum) rather than a predominance of the material over the spiritual, as sounder minds would be led to assume? It would be well if these spiritualists would look down from the high stand they have chosen, and deign to believe that there are some among those experimentalists, who, clinging to matter, and gathering their facts with ant-like industry from the lowly earth, notwithstanding that they have long held communion with the poet-philosopher, Plato, and the philosophical natural enquirer, Aristotle, and have some familiarity with the Paraphrases of Hegel and Schelling, are yet unwilling to relinquish their less elevated position. If these happy admirers of their own Ideal had descended from their airy heights and closely examined organic and inorganic matter, they would not have deemed it necessary to assume, that besides carbon, hydrogen, nitrogen, and oxygen, organic substances must also contain an *organogenium* or latent vital force, or whatever else they may be pleased to call it. Had they sought information from a chemist, they would have learnt, that when exposed to the clear light of rigid logic, there is no essential difference between organic and inorganic bodies; a chemist totally unacquainted with organic matter, would *a priori* have deduced all these incidental differences of matter, from the doctrine of affinity and the science of stoichiometry, evolved from dead matter. However these advocates of a romantic poetry of nature may despise the swarm of industrious investigators, who are often unwearyingly occupied for years together in endeavouring to collect a few firm supports for the great edifice of a true philosophy of nature, we do not despair of seeing our work rise in simple grandeur, more durable and lasting than those sophisms of natural philosophy which, passing through ages from Pythagoras and Empedocles to Schelling and Hegel, have, like the sand of the ocean shore, been alternately upborne by one wave and engulphed by the next.*

The Organic Substrata of the Animal Organism.

While we admit that the general investigation of nature must derive its chief support and stability from the investigation of particulars; and while we deplore the evils that have accrued to the natural sciences from the premature abstractions and hazardous generalisations, deduced from data, which are in themselves correct; we must remember that no department of natural science, however limited its domain, should be entered upon without the aid of certain leading maxims, and without a definite aim. These must be sought by physiological chemistry in physiology, no less than in general chemistry; for without these aids zoo-chemistry will continue a confused mass of loosely connected facts, from which every fanciful enquirer may select whatever suits his views, to beguile himself or others with short-lived dreams and illusions.

The general principles and recent acquisitions of chemistry are as essential to the consideration of the properties and chemical metamorphoses of animal substances, as an intimate acquaintance with physiological theories is to the deeper insight into the chemistry of the animal functions. It would be both inappropriate, and detrimental to this branch of science, to borrow from general chemistry only such matters and facts as refer to the animal body, in order to accumulate a mass of disjointed bodies, and group them together simply according to their physiological import; as if we considered zoo-chemical processes in a purely chemical light, depending upon combination or decomposition, on chemical dualism, the theory of acids and bases, &c.: we should rather adhere in our study of the chemical substrata of the animal organism to the more general chemical points of view, from which we may consider the chemical nature of these heterogeneous substances; or, in fine, we must not leave it to chance in zoo-chemistry, whether or not we examine a chemical substance according to its occurrence in, or absence from the animal organism. We must pay special attention to the place occupied by each member of the group of chemical substances, while the contiguous members and allied substances, that may not have occurred in the same order in other animal bodies, must not be disregarded. It would be illogical to regard the metamorphic products of those animal matters that we have not hitherto been able to detect in the excreta of animal bodies, as excluded from zoo-chemistry, or at all events, as constituting only a less essential and more supplementary portion of the science. Zoo-chemistry should not only embrace, according to the principles of pure chemistry, all substances standing in a more or less intimate relation to the matters actually found in animal bodies, but it should likewise make the fullest and most extended application of the various propositions and theories by which general chemistry has at different times been enriched. At the first glance it might appear as if the physiological momentum were entirely lost in such a conception of zoo-chemistry, but so far from this being the case, we find that by such a method physiology is made to afford the greatest aid.

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* If any of my readers have chanced to meet with the article, "Chemismus in der Medicin," which appeared in the "Gegenwart," they have probably been struck by the similarity existing between the ideas expressed in the present work and the line of thought followed in that essay; I therefore feel called upon to avow the authorship of it.

The physiological importance of a body is mainly dependent on its chemical composition and quality. If this proposition be true, the assertion that a chemical conception of animal substances must likewise be a physiological one, can no longer be called in question. The physiological capacities of the material substrata of animate beings can be referred only to their chemical qualities, and no form of physiology, that was not tinctured with sophisms of the spiritualist school, could hold that a chemical substance should depose all its integral properties in the animate body, to assume higher or more spiritual capacities in the vital sphere. But while we would endeavour in the following pages to establish the principle of the purely chemical arrangement of zoo-chemical substances, we at the same time most fully award to physiology what is its due. A chemical arrangement of animal substances must be in perfect accordance with a physiological one; while the latter would neither be rational, correct, or in accordance with nature, if it were to associate substances having different chemical qualities, and artificially separate others of analogous chemical characters. Thus, it is self-evident, that substances containing no nitrogen, as starch, sugar,

&c., must be associated with very different physiological functions from albuminous bodies, containing a large quantity of nitrogen: but we should hardly have expected that the difference between nitrogenous and non-nitrogenous bodies should be so clearly shown in the two great kingdoms of living organisms; the vital phenomena of animals and plants, in a great measure owe their differences to the diversity of these two classes of chemical substances. We shall find in the course of our observations, that pure chemistry cannot sever or group together organic substances, otherwise than as physiological conditions shall require.

When we speak of applying a purely chemical principle to the classification of the objects embraced in zoo-chemistry,—understanding by the term, the theory of the chemical substrata of animal organisms,—we do not refer to the old and bye-gone classification of organic substances into acids, bases, and indifferent or amphoteric bodies; for we are of opinion that a classification of animal substances, according to their combined chemical relations and their chemical import, (but not according to a single property, as for instance their basicity or acidity), must be physiologically correct, since it is a natural method of arrangement. On the other hand we regard a purely physiological principle of classification in zoo-chemistry (such as we followed in the first edition of the present work) as no less irrational and unnatural than that which has originated in views based merely on a theory of affinities. Although we might at first sight be disposed to regard as appropriate a classification of organic substrata into nutrient matters and excreta, the practical application of such a mode of treatment will exhibit numerous deficiencies, which completely nullify the advantages it might have been supposed to possess. For it soon becomes apparent, that a body which appears in one part of the animal organism, or in one process, strictly as a product of decomposition, is applied in another to the formation of a tissue, or the accomplishment of a purely physiological function. A separation of zoo-chemical substances into secreted and excreted matters, leads to the greatest uncertainty and the most intricate confusion. We must, however, admit that every systematic mode of arrangement seems impracticable in a purely empirical science, which ought only to follow a genetic or ætiological, and not a teleological method; since the latter can, at most, only indicate the direction in which investigation should be pursued in an immature science. A new phrase has, however, been recently employed by which it was conjectured that zoo-chemical processes might, according to their nature, be separated into two wholly different classes, viz. progressive and regressive metamorphosis of matter. However deserving these words may be of being retained in physiological chemistry to serve as concise and generalising designations, they do not express definite ideas in relation to the abstruser study of this science, or of pure zoo-chemistry. Without dwelling upon the fact that it is impossible to prove, in the case of many zoo-chemical substances, whether they belong to the progressive or the regressive metamorphosis of matter, we will only observe, that even in the animal processes no limits can be drawn between the termination of progressive and the commencement of regressive metamorphosis. Carnivorous animals only introduce into their organism well-elaborated animal matter, and hence in them the extent of the progressive metamorphosis must be very inconsiderable; yet an opinion has long been entertained, that in animal life there is a regressive formation alone, and in vegetable life only a progressive development of organic matter. The acrimonious discussion that arose, as to whether the fibrin of the blood belonged to the progressive or the regressive metamorphosis, is sufficient proof that no leading principle is embodied to these terms. We perceive, therefore, that a purely physiological mode of classification is as untenable as those chemical methods which have been borrowed from the individual, and, in most cases, incidental properties of substances.

No chemist at all acquainted with the present state of organic chemistry, will be disposed to place such bodies as albumen and urea in one genus, because both these substances are nitrogenous and amphoteric, any more than the physiologist, who is well aware that a nutrient substance must of necessity have a very different chemical constitution from an excreted substance. We would, therefore, again observe that chemists and physiologists must perfectly coincide in their views respecting the mode of classifying and considering animal bodies, and that where they differ in their description, both cannot be true to nature; for where, for instance, a physiologist should regard a substance as a product of secretion, while the chemist classed it with albuminous substances in accordance with his observation of its constitution, one or the other must be in error; since the chemical qualities of a body cannot be at variance with the physiological. That method which fulfils the requirements of both sciences, chemistry as well as physiology, can therefore be the only correct mode of treating zoo-chemistry.

Although zoo-chemistry constitutes the firmest basis of physiological chemistry, and although the chemical element should be duly considered, we ought not wholly to lose sight of the physiological relations of individual substances. It is not enough to describe the properties, composition, preparation, and decomposition of matters without also considering their physiological character. The occurrence of a substance in certain parts of the animal body and in certain processes, its relation to the general metamorphosis of matter, and its progressive or regressive formation, are all questions for whose solution we do not look to pure chemistry, although physiology alone is equally incompetent to the task.

A structure such as we have endeavoured to sketch, appears to us indispensable to zoo-chemistry, before we can expect that physiology and medicine will furnish an exact reply to those general questions in chemistry which refer to the more important processes. Similar views have undoubtedly guided most true natural enquirers in their labours in this field of scientific investigation. Nor have such men as Berzelius, Wöhler, Liebig, and Mulder, ever undertaken investigations which from their deficiency in all scientific bases could not lead to any scientifically reliable results. We find that such men have always endeavoured to afford that internal scientific support to pure zoo-chemistry without which it must continue a mere medley composed of disjointed facts. In the present day we are, however, justified in expecting well-grounded physiological results from pure zoo-chemistry, nor do we exaggerate in stating that more light has been thrown on the metamorphosis of animal matter by such zoo-chemical investigations, as Mulder's on albuminous substances, Liebig's on creatin, and Wöhler's on uric acid, than by many hundred analyses of the blood and urine.

In accordance with the views already advanced, we shall in the following sketch of the zoo-chemical elements, retain those groups that have been established by the most recent investigations of pure chemistry. Bodies of homologous chemical value must also possess common physiological relations. We shall begin with bodies of the simplest composition, most of which have seldom, if ever, been found developed in the animal organism; but with which it is necessary we should become acquainted as the derivatives of animal substances. By thus passing from the groups of simply constituted bodies to those of more complicated composition, we shall gradually become more familiar with the mechanism of the association and separation of organic matter, until we are finally enabled to form a correct judgment of the most complicated substances of the animal organism. We must, however, submit the facts before us to a careful and critical enquiry, if we would employ zoo-chemistry as the firmest support of physiological chemistry. For there is scarcely any department of scientific enquiry in which truth and error, suppositions and facts, acquired and presumed results, and positive and hypothetical deductions, have been more confounded. We need only refer to the fanciful trifling with chemical formulæ which, from bearing the impress of the words and symbols of an exact science, have deceived many unaccustomed to such characters. The cause of the many erroneous views which have passed from physiological chemistry to physiology and medicine, mainly depends upon the inadequate knowledge of what is necessary for *the establishment of a formula for the chemical constitution of a body.* It seems, therefore, not wholly inappropriate, in an introduction to zoo-chemistry, to refer to the points in pure chemistry, from which alone the chemist is able to deduce a formula.

We might indeed draw some conclusions regarding the atomic composition of a body from the mere result of one or more elementary analyses, or, in other words, we might, from the percentage composition of a body, construct an empirical formula which would serve to exhibit the relation of the separate elements to one another. But this method can alone possess any scientific value when, on the one hand, we are convinced that the substance under consideration is chemically pure, and when,on the other hand, after the former fact has been fully proved, the errors incidental to every analysis are considerably smaller, (*i. e.* when the variations in the percentage results of the analysis are less,) than would be afforded by any other formula than the one calculated. Such variations by which an entire analysis may be rendered unavailable are of common occurrence in the determination of hydrogen; the atomic weight of this element being so small that the slightest variations in the percentage composition derived from the individual analyses may cause the formula of a body to differ by one or more atoms of hydrogen. Moreover, another reason why elementary analyses often exhibit the most marked variations in the quantity of hydrogen, is that the drying of an organic substance is only relative, and as many of these substances are extremely hygroscopic, it is impossible, even with the greatest care, to prevent them from condensing water from the atmosphere during the process of weighing. We call this drying relative, because in many substances we are unable to determine at what degree of temperature, and after what time they should be regarded as dried, as decomposed, or as still retaining water. Hence it is evident that the number of atoms of hydrogen will be computed with the least certainty in the most important elements of zoo-chemistry, as in the albuminous matters and their derivatives, which are bodies of very high atomic weight.

In consequence of the atomic weights of these substances being so high, and considering the great uncertainty whether they are free from all admixtures, excepting the salts with which they are inseparably connected, the number of atoms of carbon cannot be computed with certainty from the empirical result of the analysis. As, moreover, we possess no means of directly determining the oxygen contained in an organic body, and can only estimate it by the loss in weight of the substance analysed, that is to say, by the subtraction of the quantities of carbon, hydrogen, and nitrogen, the collective errors in the investigation will frequently affect the number representing the oxygen, which must therefore be regarded as the most uncertain number in the analysis.

When all the errors which attach to the calculation of atomic formulæ from the direct results of elementary analyses have been as thoroughly as possible avoided, and even when they may be regarded as $= 0$, the formula will still only have a *problematic value* until the saturating capacity of the body has been determined by direct experiment, that is to say, until the atomic weight derived from the saturating capacity of the body shall be found to accord with that deduced from the analysis. We have therefore no guarantee for the true atomic weight of a body, or for its atomic composition, without a previous knowledge of the saturating capacity, even supposing that all the other data were perfectly correct, and free from doubt. Thus, for instance, we should not know whether lactic acid and starch were composed according to the formula $C_6H_5O_5$, or $C_{12}H_{10}O_{10}$, or according to other multiples. But there are, unfortunately, many animal substances of a higher order, whose atomic composition cannot be tested by a comparison with their saturating capacity. Such substances either do not combine in definite proportions with other substances, or do so in various relations, so that it is impossible to determine which combination is actually to be regarded as the neutral one. The variations in the numbers of the saturating capacity, are frequently much more important in such bodies (partly owing to the admixture of mineral substances with them) than those of the numbers of the elementary analysis; that is to say, the atomic weight derived from the saturating capacity is frequently no less uncertain than that derived from the elementary analysis.

If these well-established rules be followed, and the properties of most albuminous matters and their derivatives be compared in accordance with these considerations, we shall easily perceive what credit should be attached to the formulæ established for the composition of these bodies, and with what temerity these most problematic of all formulæ have been transferred to physiology only to involve it in a new labyrinth of vague dreams and fantastic fictions. This absence of reasoning power, this perfect ignorance of all leading maxims having any scientific import, this superficial knowledge of the true requirements of science, has led many physicians to make elementary analyses of admixtures of several substances of a highly variable composition: as, for instance, of blood, bile, muscle, &c., and to establish chemical formulæ from the data thus afforded. Even were it not known that these animal fluids are composed in their physiological condition of constituents having very variable and different proportions, and that microscopic observation had shown the muscular bundles to be composed of very distinct and separate morphological elements, this offence against the first principles of chemistry ought not to be palliated, on the supposition that unchemical experiments might chance to yield valuable physiological results; for physiology demands from chemistry exact and scientifically established facts, and not the mere *ignes fatui* of chemical illusions.

NON-NITROGENOUS ACIDS.

$$=C_nH_{n-1}O_3+HO.$$

The acids of this group possess (as is indicated by the above formula) the following property; in their isolated state, that is to say when not combined with bases, they contain 4 atoms of oxygen and a multiple of a carbo-hydrogen polymeric with olefiant gas; in their combination with bases they lose, however, 1 atom of water, so that the resulting salt contains an acid in which 3 atoms of oxygen are combined with a carbo-hydrogen whose hydrogen is always too little by 1 equiv. exactly to produce olefiant gas with the carbon.

The number of this class of acids is considerable; we have

Formic acid	$C_2H\,O_3.HO=(CH)_2O_4$.
Acetic acid	$C_4H_3O_3.HO=(CH)_4O_4$.
Metacetonic acid	$C_6H_5O_3.HO=(CH)_6O_4$.
Butyric acid	$C_8H_7O_3.HO=(CH)_8O_4$.

Valerianic acid	$C_{10} H_9 O_3. HO=(CH)_{10} O_4$.
Caproic acid	$C_{12} H_{11} O_3. HO=(CH)_{12} O_4$.
Œnanthylic acid	$C_{14} H_{13} O_3. HO=(CH)_{14} O_4$.
Caprylic acid	$C_{16} H_{15} O_3. HO=(CH)_{16} O_4$.
Pelargonic acid	$C_{18} H_{17} O_3. HO=(CH)_{18} O_4$.
Capric acid	$C_{20} H_{19} O_3. HO=(CH)_{20} O_4$.

Closely approximating to them in their composition is another somewhat extensive group of organic acids, the "fatty acids." which, however, we shall consider separately, because they possess certain distinctive characters which would interfere with the general view which we propose to take of these acids.

It is not surprising that as these acids present a perfect analogy in their composition (homology), they should also present very many similarities in their physical and chemical properties. They are all fluid at an ordinary temperature, and, when freed as much as possible from water, are mostly oleaginous; they do not crystallise and solidify at a higher temperature than 0°, but are so volatile that at an ordinary temperature they more or less powerfully irritate the eyes and nostrils; they are colourless, but have a peculiar burning or acrid taste. They are soluble in almost every proportion in water, alcohol, and ether; they redden litmus powerfully; they may be distilled without being decomposed; their boiling point ascends with the number of the atoms of the carbo-hydrogen (according to Kopp, at the rate of 19° [34°·2 F.] for 2 atoms of CH), and the densities of the vapours of these acids have a similar relation to the number of the atoms of the carbo-hydrogen; moreover these vapours are inflammable when too much aqueous vapour is not mixed with them.

Combined with bases, these acids form salts which are for the most part soluble, and some of which crystallise readily. With organic haloid bases,—the oxides of methyl, ethyl, amyl, and lipyl,—they form what are called haloid salts, which are produced either by direct union of the acid and the base, or by double decomposition. Almost all the compounds of the first three are liquid, and extremely volatile; their boiling point is lower by a definite number of degrees than that of the corresponding acids when deprived as thoroughly as possible of water. In no class of bodies have so large a number of metameric substances been hitherto found as in this; thus, for instance, metacetonic acid=$C_6 H_5 O_3. HO$, formiate of oxide of ethyl.=$C_4 H_5 O. C_2 HO_3$, and acetate of oxide of methyl=$C_2 H_3 O. C_4 H_3 O_3$, containing equal numbers of the atoms of the individual elements=$C_6 H_6 O_4$, are metameric; so also are œnanthylic acid$=C_{14}H_{13}O_3.HO$, acetate of oxide of amyl$=C_{10}H_{11}O.C_4H_3O_3$, caproate of oxide of methyl$=C_2H_3O.C_{12}H_{11}O_3$, and valerianate of oxide of ethyl$=C_4H_5O.C_{10}H_9O_3=C_{14}H_{14}O_4$.

Most of these acids were formerly called *volatile fatty acids* from having first been made known through the decomposition of many fats; but this designation ought no longer to be retained, because while a large number of these acids cannot be prepared from fats, others again may be obtained with equal facility, as educts and products of many other animal or vegetable substances. Thus, for instance, butyric acid, which was formerly regarded as the representative of these acids, may be as easily obtained by the putrefaction or artificial oxidation of albuminous substances, or by the fermentation of sugar and starch, as by the saponification of butter.

Before we enter upon the consideration of the individual acids belonging to this group, we must draw attention to some of the relations possessed in common by all of them, and which depend upon the substances with which they are intimately connected, upon the series of homologous bodies from which they are either produced, or into which they are converted under like conditions, and more especially upon their chemical constitution.

We would first draw attention to the fact that by following the theory of organic radicals, we discover a number of bodies which may be regarded as lower stages of oxidation of the carbohydrogen radical of these acids. Thus we have bodies of the general formulæ $C_nH_{n-1}O+HO[=(CH)_nO_2]$ and $C_nH_{n-1}O_2+HO[=(CH)_nO_3]$. The substances composed in accordance with the first of these formulæ have been named oxides of the radicals of the acids, or more commonly aldehydes. These bodies are for the most part liquid, very volatile, and oxidise rapidly when exposed to the air, becoming thus converted into their corresponding acids. Up to the present time, the following bodies of this classhave been accurately studied.

Aldehyde of acetic acid	$C_4H_3O.HO$.
Aldehyde of metacetonic acid	$C_6H_5O.HO$.
Aldehyde of butyric acid	$C_8H_7O.HO$.

The stage of oxidation$=C_nH_{n-1}O_2.HO$, existing between these oxides and the acids in question, is only found in a few cases; as

Acetylous acid	$C_4H_3O_2.HO$.
Œnanthylous acid	$C_{14}H_{13}O_2.HO$.

Moreover they are rapidly oxidised by the air, and converted into the corresponding acids.

From the dry distillation of the baryta-salts of several of these acids, substances isomeric with the aldehydes have been obtained. They are known by the terminal syllable *al;* they occur as oily, very volatile, pungent fluids, which can be distilled without undergoing decomposition, dissolve freely in alcohol and ether, but not in water, possess neither acid nor basic properties, are not so easily converted into the corresponding acids by the action of the atmosphere as by means of oxidising substances, and readily exchange a portion of their hydrogen for chlorine. At present we are acquainted with—

Butyral	$C_8 H_8 O_2$.
Valeral	$C_{10}H_{10}O_2$.
Œnanthal	$C_{14}H_{14}O_2$.

Another series of derivatives is obtained from these acids by heating their salts with strong bases, the acid losing the elements of an atom of carbonic acid, and becoming converted into a substance which, in addition to a carbo-hydrogen polymeric with olefiant gas, (but composed of an odd number of atoms,) contains 1 atom of oxygen; thus, for instance, $Ca\,O.\,C_8\,H_7\,O_3 - C\,O_2 = C_7\,H_7\,O$. These bodies are distinguished by the terminal syllable *one;* they are colourless and very volatile oils with a penetrating odour, readily soluble in alcohol and ether, insoluble in water, very inflammable, and not capable of combining with acids or bases.

In these acids, as in many other organic bodies, certain atoms of hydrogen may be replaced by the corresponding number of atoms of chlorine, bromine, or iodine; thus, for instance, the formation of chloracetic acid is explained by the equation $C_4\,H_3\,O_3.\,HO + 6\,Cl = 3\,HCl + C_4Cl_3O_3.HO$. In butyric acid, various numbers of atoms of hydrogen may be replaced by an equal number of atoms of chlorine; thus, we have two chlorobutyric acids represented by $C_8(H_5Cl_2)O_3$, and $C_8(H_3Cl_4)O_3$. However strongly Berzelius, even to the very close of his life, may have contended against the substitution-theory, yet we must not disregard it in the consideration of the constitution of organic bodies. For although this mode of indicating the composition of organic bodies containing chlorine is opposed to the electro-chemical views that have hitherto prevailed in chemistry, it ought not to be wholly rejected, since it is the mode of representing the constitution of such bodies, which approximates most closely to the empirical composition. It necessitates no rigorous adhesion to the metaleptic views of Dumas and Laurent, if for the sake of greater facility of enquiry, and a better comprehension of the subject, we employ this mode of representation, and arrange the formulæ of these bodies so as to substitute chlorine in the place of hydrogen.

But putting out of the question the practical advantages afforded by this mode of viewing the subject, and independently of the circumstance that Berzelius's mode of indicating the composition of such bodies is very far-fetched, and cannot without great difficulty be brought in accord with other experiments, this mode of investigation is recommended by the circumstance that, in most cases, notwithstanding the loss of atoms of hydrogen, and the introduction of negative chlorine, bromine, or iodine, or of the complex atom $= N\,O_4$, corresponding to hyponitric acid, the new body retains the chemical character of the original compound; that is to say, if the mother-substance were an acid, the newly-formed substance would be so also; if it were neutral, the new compound would likewise be neutral; and it is very remarkable, that basic bodies, like the alkaloids, continue bases when the above elements, or hyponitric acid, are substituted for the atoms of hydrogen.

All the acids of this group likewise form *amide-compounds.* The term *amide* is known in inorganic chemistry. The atomic group H_2N, which cannot be exhibited in an isolated state, is found in many metallic preparations produced by treating compounds of the metallic oxides with ammonia. It might thence be assumed, that the atom of oxygen of the metallic oxide, as for instance of the oxide of mercury, has united with an equivalent of hydrogen of the ammonia to form water, and that the metal then unites with what remains of the ammonia$=H_2N$ to form the so-called amide. In organic chemistry the amides are produced in a similar manner, with this difference only, that in this department it is chiefly acid substances which have a tendency to enter into such combinations. We can best realise the production and decomposition of organic amides, by assuming that the hypothetical anhydrous ammonia-salt of the organic acids loses an equivalent of water, while an equivalent of hydrogen is withdrawn from the ammonia, and an equivalent of oxygen from the acid. Thus acetamide is equal to acetate of ammonia, *minus* 1 atom of water, since $H_3N.\,C_4H_3O_3-HO=H_2N.\,C_4H_3O_2=C_4H_5NO_2$.

According to the theory of substitutions, one atom of the oxygen of the acid in these combinations is replaced by the complex atom H_2N, but this mode of viewing the subject cannot be adopted, since the acids, by this union, entirely lose their acid character, and even basic bodies, on their entering into combination with amide completely lose their basicity. The knowledge of these amide-compounds, and of their general characters, which have only recently attracted the attention of chemists, is of great importance, because there is reason for believing that several substances occurring in the animal and vegetable kingdoms belong to this class of bodies.

While the amides of many other acids can be artificially produced, by the exposure of the ammonia-salt to heat, or by the treatment of the chlorine-compounds with ammonia, the amides of the acids of this group are best obtained from their salts of oxide of ethyl and ammonia. Thus acetamide is formed on digesting acetate of oxide of ethyl (acetic ether) with fluid ammonia, since $C_4H_5O.C_4H_3O_3 + H_3N = C_4H_5O.HO + H_2N.C_4H_3O_2$.

As is shown in this formula, the oxide of ethyl becomes converted in this process into the hydrated oxide, or, in other words, the ether becomes converted into alcohol; the water necessary for this change is formed from 1 atom of the oxygen of the acetic acid and 1 atom of the hydrogen of the ammonia.

The amides of these acids are solid, crystallisable, and colourless; they are soluble in water and alcohol, sublime without undergoing decomposition, have no action on vegetable colours, and are indifferent towards weak acids and bases. If, however, they be treated with strong acids or bases, they assimilate water and become decomposed into ammonia and the corresponding acid.

Acetamide, treated with caustic potash, yields ammonia and acetate of potash: $C_4H_5NO_2 + KO.HO = KO.C_4H_3O_3 + H_3N$.

The behaviour of this amide, as well as that of all others, towards nitrous acid, is very characteristic; for, by the action of this acid, these amides are converted into the original acids, ammonia being at the same time developed. (Piria.*)

We may explain this process by supposing that hydrogen is assimilated through the action of the nitrous acid on the amide, and that ammonia and the organic acid are formed, the ammonia, however, *in statu nascenti*, becoming decomposed with the nitrous acid into water and nitrogen; thus, for instance, acetamide and nitrous acid yield water, acetic acid, and nitrogen, for $C_4H_5NO_2 + NO_3 = C_4H_3O_3 + 2\ HO + 2\ N$. In this way we may hope that several nitrogenous animal matters may be discovered to be amides, as in the case of asparagin, which has been shown to be the amide of malic acid.

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* Ann. de Chim. et de Phys. 3 Sér. t. 22, pp. 170-179.

If the amides of these acids be treated with anhydrous phosphoric acid, they lose 2 atoms of water, and nitrogenous bodies rich in oxygen remain, which contain the radical of the acid and have 1 equiv. of nitrogen in place of the 3 atoms of oxygen. These bodies have been named *nitriles*. Notwithstanding the similarity of their composition with that of the volatile oxygenous alkaloids, they possess no basic properties.

Valeramide and phosphoric acid form hydrated phosphoric acid and valeronitrile: $C_{10}H_{11}NO_2+PO_5=PO_5.2HO+C_{10}H_9N$.

The amides of this group are finally distinguished by a property which is not common to the amides of most other acids; when treated with potassium they yield cyanide of potassium and a carbohydrogen. Hence it seems probable that cyanogen exists pre-formed in these amides, since, from their total want of basic properties, it cannot be supposed that they contain a conjugated ammonia and that 1 atom of oxygen can be replaced by amide.

Taking this view, acetamide must be regarded as hydrocyanate of wood-spirit, and metacetamide as hydrocyanate of alcohol, for $C_4H_5NO_2=C_2H_4O_2.HC_2N$, and $C_6H_7NO_2=C_4H_6O_2.HC_2N$.

The amides lead us at once to a further consideration of the *nitriles*, which are equally important in reference to our knowledge of the arrangement of atoms and the metamorphosis of matter.

These bodies are, in part, formed during the decomposition of animal substances by oxidising agents; they may, however, be obtained by treating the corresponding ammonia-salt or the amide with anhydrous phosphoric acid. This mode of preparation is especially applicable for the nitriles of this group of acids; others are prepared either by the mere exposure of the ammonia-salt to heat, or by passing the vapour over heated caustic lime.

The nitriles are oily, very volatile fluids, less soluble in water than in alcohol and ether, and having a peculiar odour; they can be distilled without undergoing decomposition, have no action on vegetable colours, and do not unite with acids to form salts. They unite, however, directly with sulphuretted hydrogen, assimilating 2 equivalents of it, so that sulphurous substances analogous to the amides are produced; thus, for instance, benzonitrile, with sulphuretted hydrogen, forms sulphobenzamide, which is analogous to benzamide: $C_{14}H_5N+2HS=C_{14}H_7NS_2 \sim C_{14}H_7NO_2$.

Alkalies and strong acids reduce most of the nitriles to their original component parts, that is to say, to ammonia and the corresponding acid, by assimilating 3 atoms of water; thus, for instance, in the case of valeronitrile: $C_{10}H_9N+3HO=H_3N+C_{10}H_9O_3$.

Several of the properties of the nitriles, and especially the modes in which they are decomposed, indicate that in their chemical constitution they are not to be regarded as compounds of the radical of the corresponding acid with nitrogen, but rather as combinations of cyanogen and certain carbo-hydrogens;—a view which throws a perfectly new light on the theoretical composition of the acids of this group.

If we first glance at the nitriles of the simplest acids of this group,—those of formic acid, acetic acid, and metacetonic acid,—it becomes manifest that these are bodies which have been long known, but never have been, nor can be, regarded as nitriles. The nitrile of formic acid must $=C_2HN$; this, however, is the composition of hydrocyanic acid, which, as is well known, is also obtained by heating formate of ammonia, three atoms of water being separated. Hydrocyanic acid can, however, as we know, be readily converted, like the nitriles, into ammonia and the corresponding (formic) acid.

If, farther, with the view of preparing the nitrile of acetic acid, acetamide be mixed with anhydrous phosphoric acid, another long-known body, supposed to be otherwise constituted, is formed, namely, cyanide of methyl, for $C_4H_3N=C_2H_3.\ C_3N$. The nitrile of metacetonic acid which corresponds to cyanide of ethyl, behaves in a perfectly similar manner, for $C_6H_5N=C_4H_5.C_2N$. An intelligent observer, Kolbe,* who has instituted very excellent observations on the subject, struck upon the idea of preparing metacetonic acid from the cyanide of ethyl, (obtained by the distillation of sulphate of oxide of ethyl and potash, and cyanide of potassium), by treating it with solution of potash; and the attempt completely succeeded, for the cyanide of ethyl (perfectly corresponding in its nature to the aforesaid nitrile), took up 3 atoms of water, and became decomposed into ammonia and metacetonic acid, according to the formula, $C_4H_5.C_2N+3HO=H_3N+C_6H_5O_3$.

From these facts he was led to regard the nitriles (as far as they are yet known) of the acids of this group as combinations of cyanogen with a radical of the haloid bases pertaining to the ether group, that is to say, with a carbo-hydrogen in which there are contained a large number of atoms of carbon, and the next higher odd number of atoms of hydrogen. Thus, these substances arrange themselves in the following arithmetical proportion :—

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* Phil. Mag. Vol. 31, pp. 266-271.

Nitrile of formic acid = hydrocyanic acid = $H . C_2 N$.
—— — acetic acid ... = cyanide of methyl $=C_2 H_3 . C_2 N$.
—— — metacetonic acid = cyanide of ethyl $=C_4 H_5 . C_2 N$.
Butyronitrile .... $=C_6 H_7 . C_2 N$.
Valeronitrile .... $=C_8 H_9 . C_2 N$.

While in the first three of these combinations the existence of cyanogen may be regarded as established, Kolbe* believed that he could recognise the existence of such carbo-hydrogens as C_6H_7 and $C_8 H_9$; and, indeed, he fully proved their presence, by exposing to an electric current the potash-salts of the acids corresponding to the two last-named nitriles, namely, butyric acid and valerianic acid; besides other products, he then obtained the carbo-hydrogens $C_6 H_7$ and $C_8 H_9$. In further investigations,† by decomposing cyanide of ethyl by potassium, he established the existence of the radicals, methyl and ethyl, C_2H_3 and C_4H_5.

From these facts relating to the nitriles of these acids, we are almost involuntarily led to Kolbe's original view, and to regard the acids of this group as conjugated oxalic acids, that is to say, as acids in which oxalic acid is so combined with one of the above-named carbo-hydrogens$=C_nH_{n+1}$, as not to affect the saturating capacity of the acid.

This view is supported by the following experimental evidence.

Butyric and valerianic acids are decomposed under the influence of the galvanic current; assimilating an atom of oxygen, they yield 2 equivs. of carbonic acid and the corresponding carbo-hydrogen.

Cyanogen with water becomes decomposed, as is well known, into oxalic acid and ammonia ($C_2N+3HO=H_3N+C_2O_3$); conversely, on heating oxalate of ammonia, cyanogen, together with oxamide, is formed. The production and decomposition of valeronitrile may hence be explained in the following manner : if valerianic acid be an oxalic acid conjugated with the carbo-hydrogen, *valyl*$=C_8H_9$, the latter is converted into cyanogen by the metamorphosis of the ammonia-salt into nitrile; and the cyanogen combining with the adjunct C_8H_9, yields the empirical formula for valeronitrile. If, however, the latter be regarded as cyanide of valyl, and be decomposed by alkalies, the conjugated cyanogen, just as if it were isolated, becomes converted into ammonia and oxalic acid, which then remains in combination with the conjugate C_8H_9.

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* Chem. Gaz. Vol. 5, p. 228.

† Ann. d. Ch. u. Pharm. Bd. 65, S. 271-288.

Considering the subject in this point of view, we must regard the acids of this group as constituted in the following manner:—

Formic acid =hydrogen-oxalic acid= $H.\ C_2O_3$.
Acetic acid =methyoxalic acid $=C_2H_3.\ C_2O_3$.
Metacetonic acid =ethyloxalic acid $=C_4H_5.\ C_2O_3$.
Butyric acid =metethyoxalic acid $=C_6H_7.\ C_2O_3$.
Valerianic acid =valyloxalic acid $=C_8H_9.\ C_2O_3$.
Caproic acid =amyloxalic acid $=C_{10}H_{11}.C_2O_3$.

Closely allied to this view of the constitution of these acids is another consideration, which has reference to the production of these homologous acids from the series of the ether-like, homologous haloid bases. The general formula of the haloid bases,—oxide of methyl, oxide of ethyl, and oxide of amyl, is$=C_nH_{n+1}O$, while the formula of the acids is $C_nH_{n-1}O_3$; we have explained the production of the acids from the corresponding haloid bases by the simple assimilation of 4 atoms of oxygen, and loss of 2 atoms of water; as, for instance, in the conversion of oxide of ethyl into acetic acid: if, however, the above conclusions, which have been derived from simple inductions, be correct, it must be assumed that (to take a definite case) in the conversion of oxide of ethyl into acetic acid, the complex atom, C_2H_2, leaves the radical of the oxide of ethyl, C_4H_5O, and unites with 4 extraneous atoms of oxygen, and with the 1 atom which is present in oxide of ethyl, to form water and oxalic acid, which combines with the radical of the next lower haloid base, methyl, and represents acetic acid.

Oxide of amyl yields valyloxalic acid:

$$(C_{10}H_{11})O+4O=2HO+(C_8H_9)\ C_2O_3.$$

Oxide of valyl yields metethyloxalic acid:

$$(C_8H_9)O+4O=2HO+(C_6H_7)C_2O_3.$$

Oxide of metethyl yields ethyloxalic acid:

$$(C_6H_7)O+4O=2HO+(C_4H_5)C_2O_3.$$

Oxide of ethyl yields methyloxalic acid:

$$(C_4H_5)O+4O=2HO+(C_2H_3).C_2O_3.$$

As, according to this view, oxalic acid constitutes the acidifying principle of the bodies of this group, we shall consider it the first in the series of acids.

OXALIC ACID.—$C_2O_3.HO$.

Chemical Relations.

Properties.—This acid crystallises with 3 atoms of water in oblique rhombic prisms, is devoid of smell, has a sharp acid taste, and effloresces on exposure to the air, losing 2 atoms of water and becoming disintegrated into a white powder; on heating it carefully to 150° or 160°, it sublimes undecomposed in acicular crystals; but at 170° (or if the crystallised acid be rapidly heated to 155°), it becomes decomposed into carbonic oxide and carbonic acid, a little formic acid, and water; it dissolves in 8 parts of cold and 1 part of boiling water, and in 4 parts of spirit of wine; its solutions redden litmus strongly. On boiling oxalic acid with solution of oxide or chloride of gold, carbonic acid is evolved, and the gold is precipitated in the form of extremely fine black powder. Treated with concentrated sulphuric acid, it becomes decomposed into carbonic oxide and carbonic acid, and effects no change in the colour of the sulphuric acid.

Composition. In accordance with the above formula, this acid, which cannot exist in the free state without water, contains in 100 parts:

Carbon	2 atoms	=	26·667
Hydrogen....	3 „	=	53·333
Water	1 „	=	20·000
			100·000

The atomic weight of the hypothetical anhydrous acid$=450·0$; its saturating capacity$=22·222$.

In reference to the history of this acid, we may observe that while some chemists regard it as the oxide of an oxygenous radical, oxalyl$=C_2\,O_2$, in consequence of the preponderance of its acidity over that of carbonic acid, others regard it as a hydrogen acid $=C_2\,O_3\,.\,H$.

Combinations. Oxalic acid combines with alkalies in three proportions, in which the oxygen of the base is to that of the acid as 1 : 3, 1 : 6, and 1 : 12 respectively. These salts are soluble in water, but all other oxalates are insoluble, or only very slightly soluble, in that fluid; none of the oxalates are soluble in alcohol. These salts do not char when heated. The combinations of oxalic acid with the more easily reducible oxides, yield carbonic acid and the reduced metal (thus, for instance, $CoO.C_2O_3=2CO_2+Co$); while those with less easily reducible bases evolve carbonic oxide gas, and are converted into carbonates.

Oxalate of Ammonia, neutral oxalate of oxide of ammonium,

$H_4NO.C_2O_3+2HO$, is obtained by neutralising oxalic acid with carbonate of ammonia, and evaporating the solution; it crystallises in needles, has a saline taste, effloresces on exposure to the atmosphere, and its solubility in water is less than that of oxalic acid.

Oxamide, $C_2H_2NO_2(=H_2N.C_2O_2)$ is obtained either by the dry distillation of oxalate of ammonia, or by the treatment of neutral oxalate of oxide of ethyl with ammonia; it has a crystalline powdery appearance, is of a glistening white colour, has no smell or taste, and dissolves very slightly in cold, but rather more freely in hot water; when strongly heated it becomes decomposed into water, carbonic oxide, hydrocyanic acid, and a little urea. If a sufficient quantity of water be present, a very small quantity of oxalic acid can convert an infinite quantity of oxamide into oxalate of ammonia.

Oxamic Acid, $C_4H_2NO_5.HO$, is an acid in which we assume that oxalic acid is conjugated with oxamide ($C_2H_2NO_2.C_2O_3.HO$); it is produced by the dry distillation of binoxalate of ammonia; it occurs as a colourless granular inodorous powder, which is not readily soluble in water, and reddens litmus. When heated with sulphuric acid it becomes decomposed into ammonia and oxalic acid; its salts are for the most part soluble; at least its baryta, lime, and silver salts dissolve in boiling water.

Oxalate of Lime, $CaO.C_2O_3$, is a very important substance in pathological chemistry; it occurs as a white, tasteless, and inodorous powder, which, however, under the microscope, is found to exhibit a distinct crystalline form. These crystals, whose crystallographic relations have been carefully studied by C. Schmidt*, appear, when seen with a low power, as envelope-formed, sharply defined bodies; but when more highly magnified, they may easily be recognised as obtuse square octohedra; some, however, among them, are very acute. These crystals contain 1 atom of water, which they lose at 180°. Oxalate of lime is all but insoluble in water, and it is almost proof against the action of acetic and oxalic acids; it readily dissolves, however, in the stronger mineral acids.

Artificially prepared oxalate of lime only shows these crystals, when very dilute solutions of salts of lime have been mixed with diluted boiling solutions of alkaline oxalates; under other circumstances it appears under the microscope merely in spherical or nodular masses. Crystals of oxalate of lime may be distinguished from those of chloride of sodium which they much resemble in form, by the easy solubility of the latter in water, and by their transparency. Larger crystals of oxalate of lime sometimes occur, having some resemblance to crystals of phosphate of ammonia-magnesia, which in the projection resemble a square octahedron; but a more accurate microscopic examination and the solubility of the triple phosphate in acetic acid enable us to discriminate between these crystals and those of oxalate of lime. Golding Bird[*] also describes crystals of oxalate of lime shaped-like dumb-bells or rather like two kidneys with their concavities opposed, and sometimes so closely approximating as to appear circular, the surface being finely striated. These crystals are produced, in all probability, by a zeolitic arrangement of minute acicular crystals presenting a physical structure resembling that of spherical crystals of carbonate of lime. [Dr. Golding Bird[†] has recently shown that in all probability these dumb-bell crystals consist of *oxalurate of lime*.—G. E. D.]

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* Entwurf einer allg. Untersuchungsmethode der Säfte und Excrete des thierischen *Organismus*. *Mitau u. Leipz.* 1846, S. 63-65.

Other oxalates have at present excited no physiological interest.

Preparation.—Oxalic acid is a final product of the oxidation of most animal and vegetable bodies; hence it may be prepared from very different substances by strong oxidising agents: it is most commonly obtained by the decomposition of sugar by not too concentrated nitric acid, by evaporation to crystallisation, and finally by recrystallisation in water.

Tests.—Oxalic acid and its salts are so well characterised that it is hardly possible to mistake them for any other bodies. In the animal organism oxalic acid is almost always combined with lime, and with a little practice this salt may be readily discovered by the microscope, and by the insolubility of its crystals in acetic acid. Should a further investigation appear necessary, the presence of oxalic acid might be determined by its property of reducing gold from its solutions, and by its not charring either in the free or in the combined state when heated, or on the application of sulphuric acid. Oxalate of lime can be separated from most of the substances with which it is likely to be mixed either by acetic acid or by dilute solution of potash.

Physiological Relations.

Occurrence.—Frequently as oxalic acid, combined either with the alkalies or with lime, occurs in the vegetable kingdom (Schleiden,[‡] Carl Schmidt,[§] and others), it is very seldom found in the animal organism, at least in large quantities. It only occurs in the latter in combination with lime, never being present in sufficient quantity to combine with the alkalies as well as with lime. Moreover it is much more frequently met with in pathological than in physiological conditions.

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[*] Urinary Deposits; their diagnosis, pathology, and therapeutical indications. Third edition, p. 208.

[†] Op. cit. p. 212.

Grundzüge der Botanik. 2 Aufl. 1846.

Entwurf *u. s. w.*

It is in the urine that the presence of oxalate of lime has been most frequently observed; it was for a long time regarded as a morbid product in this fluid, but independently of the circumstance that this body is constantly present, together with carbonate of lime, in the urine of herbivorous animals, it has frequently been found in normal human urine by myself,* Höfle,† and others.

In examining microscopically the morning urine of healthy men I have frequently discovered isolated crystals of oxalate of lime; this is not, however, always the case: and further, the oxalate of lime recognisable in such cases by the microscope is not all that is contained in the urine, for it forms in larger quantities after some time, and during the acid urinary fermentation so admirably described by Scherer. After allowing morning urine to stand for a considerable time we often find a great many of these crystals, when the perfectly fresh urine presented no trace of them. The following is an excellent mode of demonstrating the existence of oxalate of lime in normal urine. If it be winter we must expose fresh urine out of doors till it freezes; in this process, as in the freezing of wine and vinegar, a great part of the water crystallises in a comparatively pure state, and after its removal we obtain a concentrated saline solution in which microscopic crystals of oxalate of lime may be discovered. That oxalate of lime is at first actually held in solution in filtered urine, and that it does not, as C. Schmidt supposes, proceed from the mucus of the bladder, is a view which is supported by the experiment which I have often repeated, that in urine, which after thoroughly cooling was freed from its mucus and urate of soda by filtration, the most distinct crystals of oxalate of lime might after a time be recognised, while no traces of them could either previously be detected in the mucus of the fresh urine, or found after the residue on the filter had been for some time in contact with water. The oxalate of lime, with a few crystals of uric acid, does not separate from filtered urine until after it has stood for some time. We may very easily convince ourselves that oxalate of lime is present in a state of solution, by extracting the solid residue of filtered urine with not too concentrated spirit, and agitating the spirituous extract with ether; after the extraction with ether, there may be observed, in the alcoholic extract, a sediment insoluble in water, which consists of the most beautiful crystals of this salt. While in the acid urinary fermentation the separation of the oxalate of lime increases with the augmentation of the free acid of the urine, in the latter case the salt is separated by the removal of the free acid.

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* Wagner's Handwörterbuch der Physiologie. Bd. 2, S. 6.

† *Chemie und Mikroskop* am Krankenbette. Erlangen, 1848 S. 385.

The quantity of oxalate of lime in ordinary urine is so minute, that, till recently, chemists, from the want of sufficiently accurate means of analysis, were unable to recognise it; good analysts have, however, always found, in the insoluble part of the ash of the extract of urine, a little carbonate of lime, which, at all events, owes part of its origin to the oxalate of lime.

Crystals of oxalate of lime are most frequently found in the urine after the use of vegetable food, especially of such kinds as contain ready formed oxalates (Wilson.*) Donné found that after the use of sparkling wines, the quantity of the salt is increased in the urine; and my own experiments show that there is an increased secretion of oxalate of lime after the use of beer containing much carbonic acid and of the alkaline bicarbonates and vegetable salts. I cannot confirm Bird's view that highly nitrogenous food causes a precipitate or even an augmentation of the oxalate of lime. It is often found in the urine of pregnant women. (Höfle.)†

From a series of direct experiments on the subject, C. Schmidt‡ is led to deny that oxalate of lime introduced into the stomach, passes into the urine; and in this point I can perfectly confirm him, without, however, going so far as to assert that the food exerts no influence on the formation of this body. In the excrements of caterpillars we often find much oxalate of lime which is not formed directly from the ingesta, since I§ have very often found the crystals in the biliary ducts of these animals. Preparations can be easily made of these organs, and in consequence of their contractility a large quantity of their contents may be expressed from the cut tubes, and submitted to microscopic examination.

With reference to the occurrence of oxalate of lime in certain morbid conditions, Prout, Bird, and others, make very different statements, none of which are yet fully established. Numerous examinations of morbid urine have convinced me, that in this country, at least, the sediments of oxalate of lime are much rarer than they are represented to be by English writers. These investigations have led me to the following results; when the respiratory process is in any way disturbed, we most frequently observe a copious excretion of oxalate of lime; it is most common either in fully developed pulmonary emphysema, or when the pulmonary tissue has lost much of its elasticity after repeated catarrhs; on the other hand, it is not present nearly so often in inflammatory or tuberculous affections of the lungs (Höfle);[*] moreover, it is common in convalescence from severe diseases, as for instance, typhus, mucus-corpuscles being then often associated with a trifling sediment of oxalate of lime. [The frequent occurrence of oxalate of lime in the urine during convalescence has been independently observed by Professor Walsh. See his paper on the oxalates in the *Monthly Journal of Medical Science*, Jan. 1849. G. E. D.] I have only met with actually pure sediments of this salt in three persons, who, sometimes, (at somewhat considerable intervals), suffered from epileptic attacks. It is by no means constant, according to my experience, in the urine of rachitic children (Simon),[†] of gouty adults with osteoporosis, of women with leucorrhœa, of patients with heart-disease, or in urine containing semen. (Donné.)[‡]

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* Provincial Medical and Surgical Journal, 1846, p. 413.

† Chemie u. Mikroskop u. s. w. S. 385.

‡ Entwurf u. s. w. S. 70.

§ *Jahresbericht d. ges. Med.* 1844. S. 25.

In the dyspeptic conditions in which Prout and Bird have found sediments of oxalate of lime, I have failed in discovering anything of the sort; on the contrary, I have generally found the sediments in the urine of such patients to be free from these crystals. The reason why the English have so often found this salt in the urine, may be, that in England (as we shall further notice at a future page), the urine is generally in a more concentrated state than in Germany, and as Bird very correctly remarks, oxalate of lime is more rapidly separated from a concentrated than an aqueous urine. Moreover, experience at the bed-side teaches every unprejudiced observer that the appearance of oxalate of lime in the urine is by no means accompanied by the group of symptoms which certain English physicians describe as pertaining to what they call the oxalic diathesis. [For the arguments in opposition to this opinion the reader is referred to Dr. Golding Bird's *Urinary Deposits*, 3rd Ed., p. 230. G. E. D.]

That the mulberry calculus consists for the most part of oxalate of lime, has been long known; but most other urinary calculi, whether they consist principally of earths or urates, almost always contain a little oxalate of lime.

This salt has only rarely been found in other places besides the urine. C. Schmidt has remarked that it is often present in the mucus of the gall-bladder, and that it is scarcely ever absent from the mucous membrane of the impregnated uterus. I once discovered oxalate of lime in expectorated matter, but whether it was produced from the pulmonary mucus, or from fragments of food in the mouth, I could not decide. [Dr. Garrod* has recently detected oxalic acid in the blood in a case of chronic hiccup and vomiting, and in several cases of gout. G. E. D.]

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[*] Chemie u. Mikroskop u. s. w. Nachtrag, S. 176.

[†] Hufeland's Journal, 1841. Dec. S. 73-88.

[‡] *Cours de microscopie*. pp. 249, 322.

Origin.—As the use of vegetable food, of which many varieties contain oxalates, increases the quantity of oxalate of lime in the urine, the inference would seem a legitimate one, that the oxalates are transmitted from the food to the urine. The source of this salt must, however, not be sought for only in the pre-formed oxalates, but in the amount of alkalies in combination with vegetable acids present in the food; for, as we have already mentioned, they induce an augmentation of the oxalate of lime. In all the well-marked cases to which I have alluded, the increase of the oxalate of lime seemed to be combined with disturbance of the respiratory process. Thus it may easily be understood why, after the use of drinks rich in carbonic acid, of alkaline bicarbonates, or vegetable salts, oxalic acid is increased in the urine; the superfluous carbonic acid which has entered the blood, or been generated there from the salts of organic acids, must obstruct the absorption of oxygen and the perfect oxidation of certain substances in the blood; hence also the quantity of oxalate of lime has been found to be increased by the partially impeded exchange of oxygen and carbonic acid in the lungs, consequent on emphysema, pulmonary compression during pregnancy, &c. We might, in such cases, assume, according to a formerly prevalent belief, that the kidneys in some degree acted vicariously for the lungs, since under the form of oxalic acid they remove from the organism the carbon which the latter organs would have excreted as carbonic acid.

Although certain chemists hold a contrary opinion, it is an undoubted fact that the nervous system has an influence on the oxidation of the blood. The occurrence of oxalate of lime in cases of epileptic convulsions, in convalescent persons, &c., might be referred to the disturbance induced in such cases in the nutrition or in the function of the nervous system, and to its diminished influence on the process of respiration, without there being any necessity for the assumption of a special diathesis.

It seems, moreover, unreasonable to set up such a diathesis, since the establishment of a special disease from a single symptom

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* Medico-chirurgical Transactions. Vol. 32, p. 171.

—that sympton being only the occurrence of oxalate of lime—is entirely opposed to the spirit of rational medicine.

From Wöhler and Liebig's discovery that uric acid is decomposed by peroxide of lead into urea, allantoin, and oxalic acid, it has been pretty generally assumed that the oxalic acid of the urine is due to an oxidation of the uric acid; the oxalic acid, in this case, not being converted into carbonic acid, as usually occurs in the healthy organism. That the formation of oxalic acid may be in part thus explained, is unquestionable, but there are many other substances in the animal organism besides uric acid, which by oxidation yield oxalic acid. No definite numerical ratio between the uric acid, urea, and oxalate of lime in the urine, has been yet established.

C. Schmidt * has propounded a very ingenious view regarding the origin of oxalate of lime in the urine. He believes that we must seek for the source of its secretion in the mucous membrane of the urinary passages, and that the oxalate of lime is first produced by the decomposing action of the acid urine on a soluble compound, oxalate of albumen-lime, secreted by the mucous membranes; for oxalate of lime as an insoluble body could not penetrate with the urine through a series of renal cells: oxalate of lime is also formed from the mucus of the gall-bladder by this mode of decomposition. When oxalate of lime occurs in the urine, we always find an augmentation of the mucus. These reasons do not, however, appear to be so decisive as to induce us to exchange the view we have already given for that of Schmidt; and indeed in another place we find Schmidt † himself maintaining that the urea is in part combined with oxalic acid.

FORMIC ACID.—$C_2HO_3.HO$.

Chemical Relations.

Properties.—This acid possesses the general characters of the acids of this group; with water it forms two distinct hydrates, one of which becomes solid at — 1°, boils at + 99°, and has a specific gravity of 1·2353, while the other, which contains 48·35% or 2 atoms of water, does not solidify at a temperature of—15°, boils at +106° and has a specific gravity of 1·1104. By concentrated sulphuric acid it is decomposed into water and carbonic oxide ($C_2HO_3=HO+2CO$); the salts of oxide of silver and of oxide of mercury are reduced when warmed in it.

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* Ann. d. Ch. u. Pharm. Bd. 60, S. 55, ff.

† Entwurf u. s. w. S. 47.

Composition.—In correspondence with the above formula, 100 parts of this acid must contain :—

Carbon	2 atoms	26·087
Hydrogen	1 „	2·174
Oxygen	3 „	52·174
Water	1 „	19·565
		100·000

The atomic weight of the hypothetical anhydrous acid = 462·5 ; its saturating capacity=21·62. According to the theory which we have laid down, formic acid should be regarded as an oxalic acid conjugated with hydrogen=$H.C_2O_3+HO$; but according to ordinary views it is assumed to contain a radical *formyl*=C_2H, which is believed to occur in several other combinations, as for instance in chloroform.

Combinations.—The salts of formic acid are soluble; with alkalies, it also forms acid salts.

Formate of ammonia is known by its property of becoming converted on heating into hydrocyanic acid ($H_4NO.C_2HO_3= H.C_2N+4HO$), and hence the hydrocyanic acid which often appears during the decomposition of animal substances may be dependent on the previous formation of formate of ammonia.

There are certain combinations, which in reference to their empirical composition, may be regarded as formic acid, but in which the whole of the oxygen is replaced by chlorine, bromine, iodine, or sulphur; the best known of these is *chloroform* or *perchloride of formyl*, C_2HCl_3, which is employed in place of ether to induce anæsthesia.

Preparation.—This acid was most commonly obtained in former times by distilling a large quantity of ants with water or spirit: from the distillate, which naturally only contained the acid in a very dilute state, the concentrated acid was obtained according to the ordinary methods by saturation with a base, and by the decomposition of the crystallised salt with sulphuric acid. As, however, we have since ascertained that formic acid is a product of the oxidation of many animal and vegetable substances, we are now in the habit of obtaining it from various sources by the action of oxidising agents, as peroxide of manganese and sulphuric acid, chromic acid, or hypermanganic acid. It is best obtained by adding a little water and sulphuric acid to a mixture of three parts of sugar and one part of bichromate of potash (2 atoms of SO_3 to 1 atom of $KO.\ 2CrO_3$) and by distilling.

Tests.—This acid may be readily distinguished from most other acids by its volatility, and from other acids of this group by its power of reducing the oxides of mercury and of silver; but it must be recollected that if we obtain formic acid by the distillation of a mixture with sulphuric acid, this formic acid may have been produced by the action of the sulphuric acid on organic matter, or on already formed hydrocyanic acid. We may separate it from the other acids of this group by fractional distillation, since the boiling point of this acid is lower than that of all other homologous acids.

Physiological Relations.

Occurrence.—Formic acid has hitherto been much more frequently found as a product of the decomposition of many organic substances, as for instance in the gradual decay (Eremacausis) of coal, than as an educt of the animal body. It has only as yet been positively proved to exist pre-formed in ants (especially Formica rufa); Bouchardat and Sandras* believe, however, that they have found it in the blood of dogs which for a long time had been fed with sugar. According to Scherer,† there are contained in the juice of flesh not only lactic, inosinic, and phosphoric acids, but also formic, acetic, and several other acids of this group.

[Will of Erlangen has recently shown that the active poisonous principle in certain caterpillars is formic acid. It exists in a free, concentrated state in all parts of the animal, particularly in the fæces, in the greenish-yellow matter that exudes when the animal is cut, and in the hollow bristles. G. E. D.]

Origin.—Notwithstanding that the principal processes in the animal organism are based on an oxidation, and that, on the other hand, in the artificial oxidations of animal substances, formic acid is produced, we do but rarely meet with this acid in the animal kingdom: indeed, even with reference to the ants, it is by no means certain that they actually produce formic acid, for we know that juniper berries and the cones of several kinds of pine contain formic acid, and that these substances are much sought after by ants. We must leave this question unanswered, since it is only by direct experiments that we can determine whether ants take up exactly the same amount of acid as they yield.

Bouchardat and Sandras are of opinion that the lactic acid formed from starch and sugar in the blood is first decomposed into formic acid before its elements are finally reduced to water and carbonic acid.

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* Compt. rend. T. 20, pp. 1026 et 1085.

† Ann. d. Ch. u. Pharm. Bd. 69, S. 196-201.

ACETIC ACID.—$C_4H_3O_3$. HO.

Chemical Relations.

Properties.—Acetic acid has the general characters of the acids of this group. In its most concentrated state, as first hydrate, it forms a crystalline mass below + 16°; above this temperature it is fluid, has a specific gravity of 1·080, and boils at 117°·3; its second hydrate, containing 2 atoms of water, has a specific gravity of 1·078 and boils at 140°.

We shall notice only the most important points regarding acetic acid and its compounds, and those having an especial bearing on animal chemistry; the other compounds of acetic acid pertaining to pure rather than to physiological chemistry.

Composition.—According to the above formula, acetic acid consists of:—

Carbon	4 atoms	40·000
Hydrogen	3 "	5·000
Oxygen	3 "	40·000
Water	1 "	15·000
		100·000

The atomic weight of the hypothetical anhydrous acid $=637{\cdot}5$; its saturating capacity $=15{\cdot}686$. Kolbe's hypothesis that acetic acid is oxalic acid conjugated with methyl $=C_2H_3.\ C_2O_3.$ HO, was anticipated by Berzelius. Till then it was assumed that the radical C_4H_3 existed in acetic acid, and aldehyde and aldehydic acid were regarded as lower stages of oxidation of the same radical.

Combinations.—The only acid acetate with which we are acquainted is a potash-salt; with the oxides of the heavy metals it has a strong tendency to form basic salts.

Acetamide, $H_2N.\ C_4H_3O_2=C_4H_5NO_2$, is prepared from acetic ether and ammonia; it forms a white, crystalline, diffluent mass, which fuses at 78° and boils at 228°; it has a sweetish, cooling taste; by anhydrous phosphoric acid it is converted into cyanide of methyl; hence it has been considered as hydrocyanate of wood-spirit ($C_4H_5NO_2=C_2H_3O+HC_2N+HO$).

By dry distillation of the acetates with strong bases, we obtain *acetone* or *hydrated oxide of œnyl,* $C_6H_5O.HO$, which presents much similarity with the alcohols of the haloid bases.

On heating equal parts of acetate of potash and arsenious acid in a retort, we obtain alkarsin or oxide of kakodyl, $C_4H_6As_5O$, which is distinguished by its very specific odour.

Preparation.—The methods of producing and obtaining acetic acid are so well known that we need not here advert to them.

Tests.—Some light will be thrown on the importance of the modes of testing for acetic acid when we have to treat of the assumed or actual occurrence of acetic acid in the animal fluids.

As in the case of most organic substances, we must first separate it from most of the substances with which it is mixed, before we can apply the appropriate tests. This separation is comparatively easy because the acid admits of being distilled; hence it can only be confounded with volatile acids exhibiting reactions homologous or similar to it. It may be readily distinguished from formic acid, in consequence of the property which this latter acid possesses of being decomposed by oxide of mercury; hence these two acids can hardly be mistaken for one another. How it is to be separated and distinguished from the homologous acids, as, for instance, metacetonic acid, &c., will be explained when we treat of these acids.

If we have isolated acetic acid as completely as possible by distillation, and then by crystallisation of one of its salts, the following reactions may be established, independently of the examination of the form of the crystals; nitrate of suboxide of mercury added to a not too dilute solution of an acetate at first yields no precipitate, but, after a short time, minute crystalline specks are formed which slowly gravitate in the fluid like fatty glistening scales. Since the acetates, in common with the meconates and sulphocyanides, yield a somewhat intense red colour on the addition of a solution of a persalt of iron, acetic acid, in a mixed fluid, might be mistaken for one of these acids; but acetic acid may be readily distinguished from meconic acid by the solubility of the acetate of lime (the meconate of lime being insoluble in water), and from sulphocyanic acid by the circumstance that the red solution of sulphocyanide of iron, on the addition of ferricyanide of potassium, and on being warmed, verv soon precipitates Prussian blue, which is not the case with any other persalt of iron.

Physiological Relations.

Occurrence.—We learn from pure chemistry that acetic acid is formed in various processes of decomposition of vegetable substances—in their fermentation as well as in their dry distillation: we shall, however, presently see that it often occurs as a product of distillation of several nitrogenous animal substances. It was formerly believed that it much more frequently existed pre-formed in the animal juices than has now been shown to be the case. On this point there was formerly a controversy between Gmelin and Berzelius; the former regarding the acid which formed the soluble salts occurring in the animal fluids as acetic acid, while the latter maintained it was lactic acid; Gmelin's idea was that the volatility of the acetic acid was heightened by its combination with an organic matter. The question has finally been settled in favour of the view maintained by Berzelius.

I have never been able to recognise it as a normal constituent in any of the animal juices. Scherer has however found it, as I have already mentioned (p. 50), in the juice of flesh, together with other acids of this group. It may often occur in the gastric juice in cases of disordered digestion. In a case where, after vegetables and a little meat, but no vinegar had been taken, the vomited matters were analysed, and I satisfied myself with certainty regarding the presence of acetic acid. It has often been observed by others in vomited matters, but its presence has not always been demonstrated with sufficient chemical accuracy; for, on the one hand, vinegar or brandy might have been taken previously to the vomiting, or on the other hand, this acid might be confounded with metacetonic or butyric acid. The proof that spirit of wine is converted in the stomach into acetic acid during normal digestion, will be given when we treat of the process of gastric digestion.

Bouchardat and Sandras* think that they have sometimes discovered traces of acetic acid in the blood of animals whose food has been steeped in brandy.

The answer to the question, what change acetic acid undergoes in the animal organism when conveyed into it from without, belongs to the department of pure physiological chemistry.

Whether the acids of this group found by Scherer in the fluids of flesh have their origin in the fleshy fibre which has become effete, or whether they arise from the decomposition of other matters, and are only isolated in the muscular juice, are questions which can only be decided by further investigation.

METACETONIC ACID.—$C_6H_5O_3.HO$.

Chemical Relations.

Properties.—This acid, which has also been named *butyro-acetic acid* and *propionic acid*, forms, when in a concentrated state, a colourless, oily fluid, which at a low temperature solidifies in a crystalline form, boils at about 140°, has a peculiar sauer-kraut-like taste, and in its general character deports itself like the acids of this group; it is not perfectly soluble in a small quantity of water, but forms oily drops on it.

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* Ann. de Chem. et de Phys. 3 Sér., T. 21, pp. 448-457.

Composition.—According to the above formula it consists of:—

Carbon	6 atoms	48·649
Hydrogen	5 „	6·757
Oxygen	3 „	32·432
Water	1 „	12·162
		100·000

The atomic weight of the hypothetical anhydrous acid = 815·5; its saturating capacity=12·31.

According to the investigations of Kolbe, to which we have already referred, this acid may, or indeed must be regarded as ethyloxalic acid = $C_4H_5.C_2O_3.HO$.

Combinations.—With bases this acid forms soluble salts of a fatty and glistening appearance, some of them also conveying a fatty feeling to the touch.

Metacetonate of baryta crystallises in small rectangular octohedra or rectangular prisms with oblique terminal surfaces.

Metacetonate of silver forms glistening white granules or small prisms, which are little changed by the action of light, are difficult of solution in water, and when heated fuse, and at length noiselessly smoulder away.

Metacetonate of oxide of ethyl in contact with ammonia becomes converted into the colourless crystalline substance called *metacetamide*, $H_2N.\ C_6H_5O_2$, which, by the agency of anhydrous phosphoric acid, is converted, more easily even than metacetonate of ammonia, into cyanide of ethyl.

Metacetone, C_6H_5O, cannot be obtained from metacetonic acid, but is yielded by the decomposition of one part of sugar or starch with three parts of caustic lime; it forms a colourless, oily, volatile fluid that is essentially different from oxide of œnyl which is isomeric with it.

Aldehyde of metacetonic acid, $C_6H_5O.HO$, was discovered by Guckelberger,* among the products of distillation, during the oxidation of nitrogenous matters by sulphuric acid and peroxide of manganese; it is a colourless fluid, having an ethereal odour; its specific gravity = 0·79, it boils at about 50°, is miscible with water in every proportion, gradually becomes acid when exposed to the air, but does not reduce a solution of a silver-salt; hence, it is still questionable whether this fluid should be ranked among the aldehydes.

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* Ann. d. Ch. u. Pharm. Bd. 64, S. 46 ff.

Preparation.—Metacetonic acid is formed during the spontaneous decomposition of many vegetable substances, as, for instance, peas, lentils, and tan; by the action of hydrated potash on sugar, starch, gum, &c.; also during the fermentation of tartrate of lime in contact with nitrogenous bodies, in the decomposition of cyanide of ethyl by caustic potash; and lastly, (and, in a zoo-chemical view, this mode of its formation is the most important) in the oxidation of fats by nitric acid (Redtenbacher),* in the oxidation of albuminous bodies by chromic acid, or by sulphuric acid and peroxide of manganese (Guckelberger),† and in the fermentation of glycerin, the well known product of decomposition of the fats, by means of common yeast (Redtenbacher).‡ This acid is obtained most easily and in the purest form either by distillation of the product of the fermentation of yeast and glycerin, or by treating metacetone with chromic acid or hydrated potash; otherwise, it is ordinarily prepared by treating 1 part of sugar with 3 of hydrated potash, in which, however, it has to be separated from the other acids which are simultaneously developed, namely oxalic, formic, and acetic acids.

Tests.—Metacetonic acid must, in the first place, be separated by distillation from other non-volatile organic substances with which it may have been mixed, and then by oxide of mercury, from any formic acid that may be present. If acetic acid be also present, the best method is to combine both acids with soda, when, on evaporating the saline solution, the acetate crystallises sooner than the metacetonate. The salt which metacetonic acid forms with lead is not crystallisable, while, as every one knows, the acetate of lead crystallises very readily. How this acid is to be separated and distinguished from the remaining acids of this group, will be described when we treat of those acids. Since, however, nothing can be concluded regarding the identity of any given substance with metacetonic acid either from the forms of its salts, which have not yet been determined with crystallographic accuracy, or from the boiling point of the fluid, it is only by the elementary analysis of a pure salt that the presence of metacetonic acid can be scientifically determined.

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* Ann. d. Ch. u. Pharm. Bd. 59, S. 41-57.

† Ibid. Bd. 64, S. 46 ff.

‡ Ibid. Bd. 57, S. 174-177.

As we proceed in the subject of zoo-chemistry we shall become acquainted with a number of bodies whose characteristic properties are so feebly marked that it is only by an elementary analysis that we can satisfy ourselves regarding their presence. Often as the combustion-tube may have been mis-used in physiological chemistry, we are yet convinced that no one can flatter himself that he will advance zoo-chemistry and physiological chemistry, if he be not conversant with the methods of elementary analysis as now practised. It has unfortunately happened that physiological chemistry has too long remained in the hands of chemical *dilettanti*, who looked upon an elementary analysis as a great piece of art, and have based on the elementary analyses of others those lamentable fictions which, even yet, have hardly been eradicated from physiological chemistry.

Physiological Relations.

Occurrence.—Since acids homologous to metacetonic acid have so frequently been found in the animal system, at least as products of decomposition, we may rationally suppose that this acid may, at least occasionally, occur in pathological conditions of the organism; to this we may add that, on the one hand, metacetonic acid is, in its chemical composition, very closely allied to lactic acid, which is of such frequent occurrence in the animal body (for with 2 atoms of oxygen metacetonic acid yields lactic acid: $C_6H_5O_3.HO + 2O = C_6H_5O_5.HO$), and that on the other glycerin, (of which we are ignorant what becomes of it in the decomposition of the fats in the animal body) is so readily converted into metacetonic acid (for $C_6H_7O_5 - HO = C_6H_5O_3.\ HO$); but, unfortunately, metacetonic acid has been only so recently known to chemists, that little or no search has as yet been instituted for it in the animal organism.

BUTYRIC ACID.—$C_8H_7O_3.\ HO$.

Chemical Relations.

Properties.—This acid is an oily fluid, which remains in that state at a temperature of—20°, and can only be solidified at a cold of—113° induced by mixing condensed carbonic acid and ether, when it crystallises in plates; it evaporates even at the ordinary temperature, but it does not boil at a lower temperature than

157°; its specific gravity at 0°=0·9886; when inflamed, it burns like an ethereal oil.

Composition.—According to the above formula it consists of:

Carbon	8 atoms	54·545
Hydrogen	7 "	7·955
Oxygen	3 "	27·273
Water	1 "	10·227
		100·000

The atomic weight of the hypothetical anhydrous acid=987·5; its saturating capacity=10·126.

According to the beautiful investigations of Kolbe, butyric acid may be regarded as an oxalic acid conjugated with the carbohydrogen $C_6 H_7 = C_6 H_7.C_2O_3.HO$.

Combinations.—The alkaline butyrates are deliquescent, and not crystallisable; the compounds of butyric acid with the metallic oxides lose a portion of their acid when heated, and even at an ordinary temperature evolve a strong odour.

Butyrate of baryta, $BaO.\overline{Bu}+4HO$, crystallises in smooth prisms, grouped together in a wart-like form, and having a fatty glistening appearance; it retains its water of crystallisation at 100°, and dissolves readily in water; if thrown in small pieces on water, it assumes, like camphor, a rotatory motion till it is dissolved; further, it turns red litmus blue.

Butyrate of lime, $CaO.\overline{Bu}+HO$, crystallises in fine needles; it has the odour of butyric acid, dissolves readily in cold water, but separates almost entirely on boiling, and on dry distillation yields bodies similar to ethereal oils, namely, *butyrone*, C_7H_7O, and *butyral*, $C_8H_8O_2$.

Butyrate of magnesia, $MgO.\overline{Bu}+5HO$, forms white plates resembling boracic acid.

Butyrate of zinc decomposes on boiling into a strongly basic insoluble salt.

Butyrate of copper, $CuO.\overline{Bu}+2HO$, occurs in eight-sided, bluish-green prisms, has a strong odour of butyric acid, and is only slightly soluble in water. At a temperature of about 100° most of the acid is expelled from this salt.

Butyrate of lead does not crystallise, and is only to be obtained in a syrupy form.

Butyrate of silver forms white nacreous plates, is almost insoluble, and smoulders at a glow-heat without explosion.

Butyramide, $H_2N.C_8H_7O_2$, is obtained from butyrate of oxide of ethyl when acted on by ammonia; it forms colourless crystalline tablets, which resist the action of the atmosphere; it communicates a taste which is at first sweetish but afterwards bitter; it fuses at 115°, and at a higher temperature sublimes without change; it is soluble in water, alcohol, and ether; by anhydrous phosphoric acid it is converted into *butyronitrile*, C_8H_7N, whose theoretical formula, according to Kolbe, must$=C_6H_7.C_2N$. Butyronitrile is an oily fluid, with an agreeable, somewhat aromatic odour; its specific gravity is 0·795, and its boiling point 118°·5; treated with potassium it yields cyanide of potassium, hydrogen, and certain carbo-hydrogens.

Aldehyde of butyric acid, $C_8H_7O.HO$, has hitherto only been found by Guckelberger,[*] in the products which are obtained by the action of peroxide of manganese and sulphuric acid on albuminous or gelatinous substances. It is a colourless fluid, its specific gravity is 0·8, and its boiling point 68°; it is slightly soluble in water, but dissolves freely in alcohol and ether; it soon becomes acid when exposed to the air; it reduces solutions of the silver-salts, and, like aldehyde of acetic acid, it yields with ammonia a crystallisable compound, $H_3N.\ C_8H_7O.\ HO+10$ aq.

Butyrate of glycerin has been prepared by Pelouze and Gélis,[†] by gently heating butyric acid and glycerin with concentrated sulphuric acid, and separating the new compound from the mixture by means of water; or by passing hydrochloric acid gas through a mixture of butyric acid and glycerin; on the addition of water it separates as a yellow oil, soluble in concentrated alcohol and ether, which, when treated with caustic alkalies, again resolves itself into butyric acid and glycerin. Whether this body be identical with the butyrin (butyrate of oxide of lipyl) occurring in the fat of milk but not yet isolated, cannot at present be decided, since no elementary analysis of it has been instituted.

Preparation.—Butyric acid, which was originally discovered by Chevreul in the products of the saponification of butter, is also formed when this substance becomes rancid, and occurs amongst the products of decomposition when oleic acid is submitted to dry distillation, and especially when it is acted on by fuming nitric acid; it is likewise produced from non-fatty nitrogenous matters, as albumen, fibrin, and gelatin, during their putrefaction or their decomposition by strong oxidising agents; and, contrary to expectation, it has been found in certain processes of fermentation of non-nitrogenous bodies, as starch and sugar, where the nitrogenous admixtures only act as ferments. Lactate of lime, in the presence of nitrogenous matter, becomes converted into butyrate of lime. To obtain pure butyric acid on a large scale, we should have recourse to the last-named method. The most simple mode of procedure is to expose carob (the fruit of Ceratonium siliqua), or sugar, with sour milk and a little cheese, and with some carbonate of lime, at a temperature of 30° to 35°, as long as gas continues to be evolved, namely for five or six weeks; the filtered fluid is then decomposed with carbonate of soda, which causes a precipitation of carbonate of lime; the solution of butyrate of soda is now strongly concentrated, and, after being decomposed with sulphuric acid, is distilled; finally, the butyric acid is freed from water and acetic acid by fused chloride of calcium.

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[*] Ann. d. Ch. u. Pharm. Bd. 64, S. 46 ff.

[†] L'Institut. No. 494.

Tests.—This acid must first be separated by distillation from the non-volatile substances, as, for instance, lactic acid, with which it is not unfrequently associated; in the distillate we can then only have the acids of this group. We shall here refer to the means of distinguishing it from the acids which have been already described, namely, formic acid, acetic acid, and metacetonic acid. The first may be very easily removed by means of its property (to which we have frequently referred) of reducing the oxides of the noble metals. The acids must then be combined with soda, when the greater part of the acetate of soda may be removed by crystallisation. The soda-salts of the mother-liquid are afterwards to be decomposed by tolerably concentrated sulphuric acid, yielding in the receiver metacetonic and butyric acids, with a little acetic acid; from these the butyric acid may be pretty well separated by fractional distillation, since that which passes over at 140° is only metacetonic acid, with traces of acetic acid, and it is not till the temperature is raised to 160° or 165°, that tolerably pure butyric acid enters the receiver. If other analogous acids be also present, we must not be contented with this mode of procedure; specific as it may appear to be, we must not rely on the peculiar odour of butyric acid, but we must convert the butyric acid into one of the above-described butyrates, and after comparing the salt thus obtained with the corresponding salt of pure butyric acid, we must institute an elementary analysis, or at the least we must determine the atomic weight or the saturating capacity.

The atomic weight of the hypothetical anhydrous butyric acid is 987·5 (for 8 at. carbon$=$600·0, 7 at. hydrogen$=$87·5, and 3 at.

oxygen=300). Now if, in a baryta-salt, we have found 49$\frac{0}{0}$ of baryta and 51$\frac{0}{0}$ of butyric acid, then 49 : 51 must be the ratio in which the known atomic weight of baryta (=955·3) stands to the atomic weight of butyric acid (49 : 51 : : 955·3 : x)=994·4.

By a similar determination of the quantity of a base contained in a salt, we calculated the saturating capacity, by which, as is well known, we understand the number which expresses the quantity of oxygen contained in that quantity of base which is required by 100 parts of an anhydrous acid to form a neutral salt. Hence the saturating capacity of butyric acid is = 10·126. If we regard the above instance as an empirical result, 49 BaO saturate 51 $\overline{Bu}$, or 100 $\overline{Bu}$ saturate 96·076 BaO; in this, however, there are contained 10·06 parts of oxygen, which is a tolerably close approximation to the required number.

Physiological Relations.

Occurrence.—In the *contents of the stomach*, or rather in food which has been ejected by vomiting, we sometimes meet with a nauseous acrid or rancid-smelling volatile acid, which, beyond all question, is butyric acid. Tiedemann and Gmelin often obtained a fluid resembling butyric acid by distillation of the contents of the stomachs of sheep, oxen, and horses, fed with oats. Since the contents of the stomach can pass into the acetous, and, as we shall presently see, also into the lactic fermentation, there is nothing surprising in the circumstance of their also passing into the butyric fermentation: but even in abnormal conditions, butyric acid has not been recognised in the contents of the stomach with that absolute certainty which is as necessary in physiologico-chemical researches as in all other departments of natural enquiry.

Free butyric acid was long ago discovered in the *urine* by Berzelius, who, however, did not think that it was often to be found there. In the urine of pregnant women, and of those who, after delivery, do not suckle their children, I have sometimes found butyric acid, or, at all events, a fat which, on saponification, yielded a volatile acid, with the odour of butyric acid.

In the *sweat*, especially in that of the genitals and lower extremities of corpulent persons, we find volatile matters, with an acid reaction, and having an odour partly of butyric acid and partly of other acids of this group. Berzelius thought that the acid reaction was due to butyric acid alone, but in the present state of our knowledge it must remain doubtful whether the homologous, highly carbonaceous acids, do not occur in the sweat with or in place of butyric acid. In examining the watery extract of a night-dress steeped in perspiration, taken from a woman a few days after delivery, I found, on saponification, a rancid-smelling, volatile acid.

In the *milk*, in addition to other fats, as olein and margarin, there occurs a fat which has never yet been isolated in a state of purity, and which, on saponification, yields butyric acid, together with other acids of this group, namely, caproic, caprylic, and capric acids. The best investigations in reference to this substance were made, first by Chevreul*, in his classical work on the fats; subsequently by Bromeis†; and lastly by Lerch‡, under the direction of Redtenbacher. Even in butter there is only a little of this substance, which yields butyric acid. From 100 parts of tolerably pure butyrin, Chevreul§ only obtained 7 parts of volatile acids; Simon‖ and Herberger¶ were able to obtain only very minute quantities of volatile acids from the fat of woman's milk.

That there are fats in the *blood* which, on saponification, yield volatile acids, may be demonstrated by any one who operates with care on large quantities of the fatty matter collected from this fluid. From the blood taken from a woman within the first few days after her delivery, I obtained, by distillation with dilute sulphuric acid, volatile acids whose general properties coincided with those of this group.

[Free butyric acid has likewise been detected in the *fæces* by Ragsky and Percy.** G. E. D.]

Origin.—After what has been stated regarding the different ways in which butyric acid may be formed, we need not wonder that it is sometimes met with in the *primæ viæ;* since it may, and indeed must principally be formed from the non-nitrogenous constituents of the food. The belief that farinaceous and saccharine foods are converted into butyric acid in the *primæ viæ*, and that they thus constitute the first step in the formation of fat, is based on a fiction regarding the possible formation of fat in general, which is at present devoid of any scientific proof. No one has as yet succeeded in ascertaining the presence of butyric acid, either in the *primæ*

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* Recherches sur les corps gras.

† Ann. d. Ch. u. Pharm. Bd. 42, S. 46 ff.

‡ Ibid. Bd. 49, S. 212 ff.

§ Recherches sur les corps gras, p. 193.

‖ Frauenmilch, S. 41.

¶ Brande's Arch. Bd. 20, S. 3.

** Chemical Gazette. Vol 8, p. 104.

viæ or in the chyle; we know not what becomes of the other elements which are eliminated during the conversion of starch into butyric acid; and finally, chemically considered, butyric acid has no greater claim to the name of a fatty acid, than acetic or formic acid. We do not think that the conclusion can be justly deduced, that starch must be converted into butyric acid in order to be transformed into fat, simply because it accidentally happens that butyric acid was first prepared from a (very rarely occurring) fat, for we know that it may just as easily be obtained from albuminous bodies, and in far larger quantities from gelatin.

There is much stronger evidence in favour of the view which regards the butyric acid found in the blood, sweat, and urine, as a product of decomposition, arising from the disintegration of nitrogenous animal matters, effected by the oxygen dissolved in the juices, (in the same way as the acid is formed from these substances by artificial means,) or as probably resulting from a gradual oxidation of some of the carbo-hydrogens of the fats. This latter view is, however, only an hypothesis; but it is supported by the simplest induction. The fats are almost all combinations of fatty acids with a haloid base, glycerin or oxide of lipyl; these acids are, however, so similarly constituted to those of this group, that they have the same general formula$=C_nH_{n-1}O_3.\ HO$, with only this difference, that the carbo-hydrogens pertaining to them are expressed by higher atomic numbers (thus, for instance, margaric acid$=C_{34}H_{33}O_3.HO$). In the complicated apparatus of oxidation which we recognise in the animal organism, the fats do not burn like the oil in the wick of a lamp, but they undergo an extremely gradual oxidation, as we learn from direct experiments, which have given us a knowledge of a very large number of fatty acids, with the most varied polymeric carbo-hydrogens, or, if we please so to express it, in the lowest stages of oxidation. From experiments instituted on this group of acids, we may assume that in the gradual oxidation, $C_2\ H_2$ is always abstracted from the radical of margaric acid, and that this gradual abstraction may proceed with various degrees of rapidity, so that, in our investigations, we meet with carbo-hydrogen compounds of a lower order, which then progressively pass into the carbo-hydrogens of the acids of this group. As the radical $C_4\ H_5$ of ethyloxalic acid passes into methyloxalic acid, we are justified in believing that the radical of margaric acid passes into cetylic acid. A gradual decarbonisation of the fats must occur in the animal organism; and there are at present no scientific reasons for assuming that it takes place in any other *way than that* which has been described. We regard butyric acid, and the acids analogous to it, in so far as they occur in the animal body, as products of regressive metamorphosis of tissue, while in the different fatty acids of the vegetable kingdom the progression gradually ascends, step by step, to margaric acid.

VALERIANIC ACID.—$C_{10}H_9O_3$. HO.

Chemical Relations.

Properties.—This acid possesses the general properties of this group, has a well-known characteristic odour, an acrid burning, taste, and produces a white spot upon the tongue; it does not become solid at a temperature of $-15°$; it boils at 176°, and dissolves in 26 parts of water: it also forms a second hydrate= $\overline{Va}$. 3HO.

Composition.—According to the above formula it consists of:

Carbon	10 atoms	58·824
Hydrogen	9 „	8·823
Oxygen	3 „	23·530
Water	1 „	8·823
		100·000

The atomic weight of the hypothetical anhydrous acid=1162·5; its saturating capacity=8·602. According to Kolbe's hypothesis, its theoretical formula=C_8H_9. C_2O_3. HO.

Combinations.—The valerianates are for the most part soluble: the alkaline salts do not crystallise, but most of the other salts crystallise in nacreous plates, similar to cholesterin or boracic acid; they have a sweetish, but at the same time a valerian-like taste. Valerianic acid is separated from its salts by acetic and succinic acids, but not by benzoic acid. The *lime-salt* effloresces on exposure to the air; the *zinc-salt* dissolves in 160 parts of water, and in 60 parts of spirit of wine; the aqueous solution becomes turbid when warmed, but clears again upon cooling: moreover it reddens litmus. The *silver-salt* is very insoluble.

Valeronitrile, $C_{10}H_9N$ (or $C_8H_9 . C_2N$), was first discovered by Schlieper*, in the oxidation of gelatin by chromic acid; it may however, be obtained from valerianate of ammonia, or valeramide (H_2N. $C_{10}H_9O_2$), by anhydrous phosphoric acid. It is a thin, liquid, colourless, strongly refracting oil, smelling like alder leaves, and having a hot aromatic taste; its specific gravity is=0·81; it boils at 125°, inflames readily, dissolves in water, alcohol, and ether, and, when treated with potassium, yields cyanide of potassium, hydrogen, and carbo-hydrogens.

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* Ann. d. Ch. u. Pharm. Bd. 59, S. 1-32.

Valeral, $C_{10}H_{10}O_2$, is produced by the dry distillation of valerianate of baryta; it is a very fluid inflammable oil, which, on exposure to the air, soon becomes converted into valerianic acid.

Preparation.—This acid occurs preformed in certain plants; it is, however, like the preceding acids, a not unfrequent product of decomposition both of vegetable and animal substances: it is obtained from fusel-oil (hydrated oxide of amyl) in precisely the same manner as acetic acid is obtained from alcohol (hydrated oxide of ethyl), and from oil of valerian by simple oxidation by means of an alkali; it is formed, together with other acids of this group, from the fats by oxidising them with fuming nitric acid (Redtenbacher*); from animal nitrogenous matters, both by putrefaction (Iljenko and Laskowski†), and on decomposing them by strong oxidising agents (Schlieper,‡ Guckelberger,§ Liebig‖); and finally, if leucine be treated with caustic potash, or allowed to putrefy, it becomes converted into valerianic and no other acid, ammonia and hydrogen being evolved.

It is most easily obtained in a state of purity by the action of spongy platinum and atmospheric air on potato fusel-oil.

Tests.—In most of the ways in which valerianic acid is formed, it occurs mixed with other acids of this group; and it is as impossible in this case, as in that of the homologous acids, to detect it in a mixture by any special reagent; it must, therefore, be separated from these acids before it can be accurately examined. As its boiling point is so high, it can readily be separated from the first-described acids of this group by fractional distillation; it may still remain contaminated with butyric acid, from which it can be tolerably well separated by crystallisation of the baryta-salts, the valerianate and butyrate of baryta assuming different forms. But an elementary analysis, or a determination of the atomic weight must be made with the valerianate thus obtained, since mistakes may very easily arise between the salts of valerianic acid and those of certain acids afterwards to be described.

[Liebig¶ has recently published a paper on the separation of valerianic, acetic, and butyric acids, to which we may refer the reader. G. E. D.]

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* Ann. d. Ch. u. Pharm. Bd. 59, S. 41-57.

† Ibid. Bd. 55, S. 78-95, and Bd. 63, S. 264-273.

‡ Ibid. Bd. 59, S. 375-378.

§ Ibid. Bd. 64, S. 50.

‖ Ibid. Bd. 57, S. 127-129.

¶ Ibid. Bd. 71, S. 355.

Physiological Relations.

Occurrence.—Although this acid is so easily and so variously obtained from animal substances, it has never yet been found preformed in the animal organism; and it is a striking fact that, so far as we yet know, the acids of this group, whose amount of carbon is divisible only by 2, and not by 4, are not found in the animal organism.

We shall consequently only have occasion to refer to these acids in the following pages, inasmuch as they sometimes occur as products of the artificial decomposition of animal substances.

CAPROIC ACID.—$C_{12}H_{11}O_3.HO$.

Properties.—It is a somewhat thin liquid, with an odour resembling sweat; its specific gravity at + 26 = 0·922; it remains fluid at—9°, boils at 202°, and dissolves somewhat difficultly in ether.

Composition.—According to its formula it consists of:

Carbon	12 atoms	62·069
Hydrogen	11 „	9·483
Oxygen	3 „	20·689
Water	1 „	7·759
		100·000

The atomic weight of the anhydrous acid = 1337·5; its saturating capacity = 7·476. According to the views of Kolbe, this acid should hypothetically be regarded as amyloxalic acid = $C_{10}H_{11}.C_2H_3.HO$.

Combinations.—The caproates have the same taste and smell as the acid itself; and are mostly soluble in water and crystallisable. The *baryta-salt* crystallises in long silky needles, united in tufts, is anhydrous, and unaffected by exposure to the atmosphere; the *silver-salt* is not crystallisable, and is very difficult of solution.

Preparation.—Like butyric acid, this acid is not only formed when butter is saponified or becomes rancid, but also when oleic acid is decomposed by fuming nitric acid, and when albuminous bodies are acted on by peroxide of manganese or bichromate of potash and sulphuric acid. In the products of the decomposition of saponified butter we find caproic acid mixed with butyric, caprylic, and capric acids, which may be removed by the crystallisation of their baryta-salts. On boiling the dried mass of the baryta-salts with 5 or 6 parts of water, the butyrate and caproate are taken up, while the salts of caprylic and capric acid remain undissolved. The caproate of baryta is the first to crystallise from the solution, and the acid may easily be isolated from the salt.

Tests.—The caproate of baryta not only crystallises sooner than the butyrate, but also sooner than the valerianate, if this should happen to be present; caproate of baryta forms small clusters, consisting of microscopic prisms, while the valerianate, as we have already mentioned, appears in minute plates like cholesterin. This separation of caproic acid from its allied acids, is more easily explained theoretically than effected practically. There are no special means of determining the presence of caproic acid, except by an elementary analysis, and the determination of the atomic weight.

Physiological Relations.

Occurrence.—The remarks which we made regarding the occurrence of butyric acid in the animal organism, apply equally to caproic acid. From its peculiar sweat-like odour, it is not improbable that it exists in sweat; but of this we have as yet no proof. No one, so far as I know, has yet sought for it in the urine or in the contents of the stomach. In our observations on butyric acid we alluded to the fatty matters contained in the milk, and probably also in the blood, which, on saponification, yield this acid.

ŒNANTHYLIC ACID.—$C_{14}H_{13}O_3.HO$.

Chemical Relations.

Properties.—It is a colourless oily liquid, of a faint aromatic odour and taste; it boils at about 215°, may be distilled with only partial decomposition, dissolves slightly in water, and when inflamed burns with a clear but smoky flame.

Composition.—According to the above formula it consists of:

Carbon	14 atoms	64·615
Hydrogen	13 „	10·000
Oxygen	3 „	18·462
Water	1 „	6·923
		100·000

The atomic weight of the hypothetical anhydrous acid = 1512·5, and its saturating capacity = 6·611. Its rational formula $= C_{12}H_{13}.C_2O_3.HO$.

Combinations.—With the exception of the alkaline salts, most of its salts are difficult of solution, generally resembling tablets of cholesterin: moreover this acid has a strong tendency to form acid salts. The *baryta-salt* crystallises in nacreous scales, which are soluble in water and in alcohol.

Œnanthylous acid, $C_{14}H_{13}O_2.HO$, formerly also named œnanthic acid, occurs combined with oxide of ethyl in various fusel oils, especially in that of wine. Whether it be actually to be regarded as a lower state of oxidation of œnanthylic acid, or as a special acid, cannot at present be decided.

Œnanthal, aldehyde of œnanthylic acid, $C_{14}H_{14}O_2$, is obtained by the simple distillation of castor oil; like the other aldehydes, when exposed to the atmosphere, it readily oxidises into the corresponding acid, and forms a compound (although somewhat unstable) with ammonia.

Preparation.—This acid, which Laurent formerly discovered amongst the products of distillation of the oils, and named *azoleic acid*, is formed, together with other acids of this group, during the decomposition of wax, oleic acid, and especially of castor oil, by concentrated nitric acid. In using castor oil, however, we obtain this acid unmixed with any others, so that we have only to combine it with baryta, and recrystallise the salt, in order to obtain it in a state of purity.

Tests.—As the baryta-salt of this acid separates from the mother-liquid earlier than caproate of baryta, and more slowly than the caprylate, and as, further, it crystallises in plates, while the two latter salts form minute needles, which are grouped together so as to have a wart-like appearance, we have a means of separating, at least roughly, this acid from those which are most closely allied to it. We cannot, however, be perfectly certain regarding its actual presence, without an elementary analysis, or the determination of its atomic weight.

Physiological Relations.

Occurrence.—As has been already mentioned, this acid is only of interest in relation to animal physiology, inasmuch as it is one of the products of oxidation of the fats: and the observations which were made regarding the occurrence of valerianic acid are here equally applicable, except that œnanthylic acid is not produced during the decomposition of nitrogenous complex atoms.

CAPRYLIC ACID.—$C_{16}H_{15}O_3.HO$.

Chemical Relations.

Properties.—At the ordinary temperature this acid forms a soft, semifluid mass, which crystallises in needles below +10°, boils at 236°, has a sweat-like odour, an acid and acrid taste, is difficult of solution in water, and is inflammable.

Composition.—According to the above formula it consists of:

Carbon	16 atoms	66·667
Hydrogen	15 „	10·416
xygen	3 „	19·667
Water	1 „	6·250
		100·000

The atomic weight of the anhydrous acid = 1687·5, and its saturating capacity = 5·926. Its rational formula is $C_{14}H_{15}.C_2O_3.HO$.

Combinations.—The salts of this acid are more difficult of solution than the corresponding salts of the acids already described. Its *baryta-salt* crystallises in white granules of the size of poppy seeds, is anhydrous, resists the action of the atmosphere, and does not fuse at 100°. The *silver-salt* is white and almost insoluble. The *lead-salt* is also very difficult of solution.

Caprylone, $C_{15}H_{15}O$, was discovered by Guckelberger* among the products of the dry distillation of caprylate of baryta; it crystallises in fine needles of a silky lustre, but when fused resembles Chinese wax; it is perfectly white, fuses at 40°, solidifies at 38°, and boils at 178°, is devoid of taste, has a waxy smell, is lighter than water and insoluble in it, but dissolves readily in strong alcohol, in ether, and in ethereal as well as fatty oils. With nitric acid of 1·4 specific gravity it yields an acid nitrogenous oil (*nitro-caprylonic acid ?*).

Preparation.—We have become acquainted with this acid as a product of the saponification of butter, and as a product of the oxidation of oleic acid when acted on by nitric acid; as in the latter case it is mixed with several substances, it is best obtained by the recrystallisation of the baryta-salts of the volatile acids of butter. In the observations on caproic acid it was mentioned that the dry mass of the baryta-salts of all four acids, when treated with five or six parts of water, separates into a soluble portion containing the butyrate and caproate, and an undissolved portion, containing the caprylate and caprate of baryta. If now the undissolved portion be dissolved in boiling water and filtered while still hot, most of the caprate separates while the caprylate remains in solution. In order to effect a perfect purification, the baryta-salt must be several times recrystallised before we separate the acid from it.

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* Ann. d. Ch. u. Pharm. Bd. 69, S. 201-6.

Tests.—We must separate the caprylic acid from the other acids in the manner just described, and then determine the atomic weight.

Physiological Relations.

Occurrence.—All that has been remarked regarding the physiological relations of butyric and caproic acids applies equally to caprylic acid.

PELARGONIC ACID.—$C_{18}H_{17}O_3.HO$.

Chemical Relations.

Properties.—It is an oily, colourless fluid which at a lower temperature than + 10° becomes solid, but liquefies at and above that temperature; it has a faint odour resembling that of butyric acid, is almost insoluble in water, but communicates to it an acid reaction, and boils at about 232°.

Composition.—In accordance with the above formula it consists of:

Carbon	18 atoms	68·350
Hydrogen	17 „	10·760
Oxygen	3 „	15·190
Water	1 „	5·700
		100·000

The atomic weight of the anhydrous acid = 1862·5; its saturating capacity = 5·369; its rational formula = $C_{16}H_{17}.C_2O_3.HO$.

Combinations.—The *baryta-salt* of this acid crystallises like the valerianate and œnanthylate of baryta in glistening scales; it contains no water of crystallisation, is unaffected by the atmosphere, and is less soluble than the œnanthylate and caprylate of baryta, but rather more soluble than the caprate.

Preparation.—As this acid, unmixed with other volatile acids, occurs in the leaves of Pelargonium roseum, its preparation from that plant is preferable to that from the products of decomposition of oleic and choloidic acids by nitric acid, amongst which it was first discovered by Redtenbacher.[*] Gerhardt[†] has obtained this acid by oxidising oil of rue, $C_{20}H_{19}O_3$, with nitric acid.

Tests.—By the crystallisation of its baryta-salt we must prepare this acid so that we can make an elementary analysis and determine its atomic weight.

Physiological Relations.

The remarks already made regarding the physiological relations of œnanthylic acid are equally applicable here.

CAPRIC ACID.—$C_{20}H_{19}O_3.HO$.

Chemical Relations.

Properties.—Little is yet known regarding this acid in a state of purity, for what was formerly regarded as capric acid was a mixture of capric and caprylic acids. It constitutes a soft, greasy mass which fuses at +30°, and evolves a faint goat-like odour, is somewhat soluble in hot water, but separates on cooling in glistening crystalline particles; its boiling point is higher than that of any of the other acids of this group, but is considerably below 300°.

Composition.—According to the above formula it consists of:

Carbon	20 atoms	69·767
Hydrogen	19 „	11·046
Oxygen	3 „	13·954
Water	1 „	5·233
		100·000

The atomic weight of the hypothetical dry acid = 2037·5; its saturating capacity = 4·909; its rational formula = $C_{18}H_{19}.C_2O_3.HO$.

Combinations.—The salts of this acid are more insoluble than those of the other acids of this group. The *baryta-salt* crystallises in delicate, glistening needles; it is unaffected by exposure to the atmosphere, and contains no water.

Oil of rue, $C_{20}H_{19}O$, the ethereal oil of Ruta graveolens, may be regarded as anhydrous aldehyde of capric acid; in point of fact it is converted into capric acid by the action of nitric acid; but by more prolonged action, into pelargonic acid.

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[*] Ann. d. Ch. u. Pharm. Bd. 59, S. 41-57, and Bd. 57, S. 170-174.

[†] Ann. de Ch. et de Phys. T. 24, pp. 112-116.

Preparation.—This may be readily inferred from what has been stated regarding the preparation of caprylic acid.

Tests.—We must obtain a pure salt according to the method described in our observations on caprylic acid, and then analyse it. R. Wagner* has, however, discovered a method of detecting this acid when mixed with other substances; for on heating such a mixture with concentrated sulphuric acid, it always appears associated with its aldehyde, and on supersaturation with potash, an intense odour of oil of rue is developed.

Wagner has in this way discovered this aldehyde in butter, in cod-liver oil and other fish-oils, in old cheese, in a piece of herring, &c.

Physiological Relations.

The remarks on the physiological relations of caprylic acid apply equally to this acid.

In the saponification of butter we sometimes obtain only a single acid, *vaccic acid,* $C_{20}H_{18}O_5.2HO$ instead of butyric and caproic acids. This acid reduces silver-salts, and taking up 1 atom of oxygen, becomes converted into butyric and caproic acids ($C_{20}H_{18}O_5+O=C_8H_7O_3+C_{12}H_{11}O_3$); it undergoes the same conversion when exposed to the atmosphere, and so also does its baryta-salt.

Delphic and *hircic acids* which were formerly regarded as independent acids are probably identical with, or mixtures of some of the acids of this group.

CETYLIC ACID.—$C_{32}H_{31}O_3.HO$.

Chemical Relations.

Properties.—The body, which is also known as *ethalic acid,* forms colourless glistening needles, fuses at 57°, but is solid at 55°, may be distilled without undergoing decomposition, and is insoluble in water.

Composition.—This acid, which is isomeric with the non-volatile *palmitic acid,* obtained from palm-oil, consists according to the above formula of:

Carbon	32 atoms	75·000
Hydrogen	31 „	12·109
Oxygen	3 „	9·375
Water	1 „	3·516
		100·000

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* Journ. f. pr. Ch. Bd. 46, S. 155-157.

The atomic weight of the hypothetical anhydrous acid = 3087·5 ; its saturating capacity = 3·239. This acid which was originally discovered by Dumas and Stass,* has subsequently been accurately examined by Smith.†

If Kolbe's theory be applicable to this acid, cetylic acid must be regarded as $C_{30}H_{31}.C_2O_3.HO$, which would explain why it differs from the isomeric palmitic acid. Two isomeric acids cannot appropriately be placed in the same group; hence we place cetylic acid here instead of considering it with the solid fatty acids. We also find in this relation an additional reason why the solid fatty acids whose general formula may be regarded as $=C_nH_{n-1}O_3.HO$, should not be regarded as simple continuations or ascending members of this group.

Combinations.—The alkaline salts of this acid are soluble in water, and crystallise readily in white nacreous scales.

Preparation.—Spermaceti, from which this acid is obtained, is a haloid salt like the other fats, but instead of this acid being combined with oxide of lipyl, it is united to another haloid base entirely corresponding with the ethers of pure chemistry; this haloid base when treated with solid caustic alkalies is converted into cetylic acid. We obtain the acid which exists pre-formed in the spermaceti, by saponifying the latter with a caustic alkali, decomposing the soap with hydrochloric acid and digesting the newly formed mixture of cetylic acid and ethal ($C_{32}H_{33}O.HO$) with milk of lime; the ethal is then extracted with cold alcohol while the cetylate of lime remains. The lime-salt is then decomposed by hydrochloric acid, and the separated cetylic acid purified by solution in ether.

This haloid base, *ethal* or *hydrated oxide of cetyl*, which is obtained on the saponification of spermaceti, bears exactly the same relation to cetylic acid that alcohol bears to acetic acid or fusel oil to valerianic acid. Moreover, as we shall further more fully describe, cetylic acid may in a similar way be prepared from this body by heating one part of it in six parts of a previously heated mixture of equal parts of hydrated potash and caustic lime to a temperature of 210°—220° ; in this process, hydrogen is developed and an alkaline cetylate formed ($C_{32}H_{33}O.HO+KO+HO=4H+KO.C_{32}H_{31}O_3$) which must be purified by solution in water and crystallisation, and then combined with baryta, from which on the addition of hydrochloric acid we can separate the cetylic acid.

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* Ann. de Chim. et de Phys. T. 72, pp. 5-11.

† Ann. d. Ch. u Pharm. Bd. 42, S. 40—51.

Tests.—When the acid occurs pure and isolated, it is not difficult to distinguish it from other acids; its crystallisability and its comparatively high boiling point distinguish it from the other acids of this group, and its volatility from the solid fatty acids. On finding it in a body in which it has not been previously recognised, we should always institute an elementary analysis, and determine its saturating capacity, since it is not only possible but very probable that several similar acids remain to be discovered.

Physiological Relations.

Occurrence.—This acid has hitherto only been found in an animal fat, namely spermaceti, in combination with hydrated oxide of cetyl, and in Japanese wax (Meyer) in combination with oxide of lipyl.

Origin.—If margaric acid were actually an acid homologous to cetylic acid and to the acids of this group generally, we might easily understand that cetylic acid was produced from this acid in the same manner as acetic is formed from metacetonic acid, for margaric acid stands in the same relation to cetylic acid as metacetonic acid does to acetic acid; the difference between each pair being C_2H_2.

It is impossible at present to form any conjectures regarding the special importance of these acids in the few positions in which they are principally deposited. For a description of *hydrated oxide of cetyl* see "*haloid bases and fats.*"

NON-NITROGENOUS ACIDS.

$$=C_nH_{n-2}O_3.HO.$$

The acids of this group are only interesting in reference to zoochemistry inasmuch as, like many acids of the previous group, they are products of decomposition of very common animal matters, and especially of fats. These acids may also be regarded as conjugated oxalic acids, combined with a carbo-hydrogen isomeric with olefiant gas; at least some of the reasons which have been advanced by Kolbe in support of the theoretical composition of the preceding group, favour this hypothesis. These acids with their empirical and hypothetical formulæ are as follows:—

Succinic acid	$=C_4 H_2 O_3 . HO=C_2 H_2 . C_2 O_3 . HO$
Lipic or pyrotartaric acid	$=C_5 H_3 O_3 . HO=C_3 H_3 . C_2 O_3 . HO$
Adipic acid	$=C_6 H_4 O_3 . HO=C_4 H_4 . C_2 O_3 . HO$
Pimelic acid	$=C_7 H_5 O_3 . HO=C_5 H_5 . C_2 O_3 . HO$
Suberic acid	$=C_8 H_6 O_3 . HO=C_6 H_6 . C_2 O_3 . HO$
Sebacic acid	$=C_{10} H_8 . O_3 . HO=C_8 H_8 . C_2 O_3 . HO$

It is, moreover, worthy of remark that the acids of this group, which contain an even number of atoms of carbon, form a series very analogous to the acids of the preceding group, the acid of one series differing from the corresponding acid of the other merely by one equivalent of hydrogen.

Succinic acid	$C_4 H_2 O_3 + H =$ acetic acid	$C_4 H_3 O_3$
Adipic acid	$C_6 H_4 O_3 + H =$ metacetonic acid	$C_6 H_5 O_3$
Suberic acid	$C_8 H_6 O_3 + H =$ butyric acid	$C_8 H_7 O_3$
Sebacic acid	$C_{10} H_8 O_3 + H =$ valerianic acid	$C_{10} H_9 O_3$

Moreover, the acids of this group (like those of the preceding group) are formed when oleic acid is oxidised by nitric acid.

These acids possess the following characters in common: they crystallise readily and well, do not fuse till they attain a temperature of from 100° to 200°, and at a higher temperature they sublime in needles, developing at the same time a suffocating vapour; moreover at an ordinary temperature they are devoid of odour, have an acid taste, dissolve readily in water, alcohol, and ether, and have an acid reaction; none of them, with the exception of sebacic acid, are decomposed by boiling nitric acid; fused with hydrated potash they yield oxalic acid together with volatile products. As in the preceding group, the solubility of their salts stands nearly in an inverse ratio to the height of the atomic weight of the acid.

As these acids are only of importance in animal chemistry as products of decomposition, and belong strictly to pure chemistry, we shall restrict ourselves to the consideration of two of the most important of them, namely, *succinic* and *sebacic acids*. As, however, none of them occur pre-formed in the animal body, there is obviously nothing to be said regarding their physiological relations.*

SUCCINIC ACID.—$C_4H_2O_3.HO$.

Properties.—When perfectly anhydrous it occurs in very delicate needles which fuse at 145° and boil at 250°; with one atom of water (corresponding with the above formula) it crystallises in oblique rectangular prisms, which fuse at 180° and sublime at 250° in the form of needles or plates, containing only half an atom of water, and fusing at 160°. In other respects it has the common characters of this group.

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* [Succinic acid has recently been detected by Heintz, in a cyst containing Echinococci in the liver. See Jenaische Ann. f. Physiol. u. Med. Bd. 2, S. 180, and Poggendorff's Ann. Bd. 80, S. 118, or Chemical Gazette, vol. 7, p. 477, and vol. 8, p. 425.—*G. E. D.*]

Composition.—According to the above formula it consists of:—

Carbon	4 atoms	40·678
Hydrogen	2 „	3·390
Oxygen	3 „	40·678
Water	1 „	15·254
		100·000

The atomic weight of the anhydrous acid=625·0; its saturating capacity=16·000. Its rational formula=$C_2H_2.C_2O_3.HO$.

Combinations.—With alkalies this acid forms neutral and acid salts, which are soluble and crystallisable; with earths it forms only neutral salts; and with the oxides of the heavy metals it forms neutral and basic salts, some of which are soluble and others insoluble.

Succinamide, $H_2N.C_4H_2O_2$, is formed by the action of ammonia on succinate of oxide of ethyl; it occurs in the form of granular crystals, insoluble in cold water; like all the amides, it is decomposed by alkalies or stronger acids into the corresponding acid and ammonia.

Bisuccinamide, or *Succinimide*, $C_8H_5NO_4$, is formed on submitting succinamide to dry distillation, or on bringing dry ammoniacal gas in contact with anhydrous succinic acid; it is a white, crystallisable, fusible, soluble body, which, on being boiled with a solution of potash, takes up 2 atoms of water, and becomes decomposed into ammonia and succinic acid ($HN.C_8H_4O_4+2HO=H_3N+C_8H_4O_6$).

Preparation.—This acid was, as its name implies, originally obtained from the dry distillation of amber. It was discovered in the sixteenth century. It has since been found to exist pre-formed in certain kinds of turpentine and in certain plants. It, however, occurs much more frequently as a product of the decomposition of fats, as wax, stearic acid, spermaceti, margaric acid, &c., and in various kinds of fermentation; thus, for instance, malate of lime, in contact with nitrogenous bodies, becomes gradually converted into succinate of lime ($CaO.C_4H_2O_4-O=CaO.C_4H_2O_3$).

According to C. Schmidt,* succinic acid is found in greater or lesser quantity in all fermented fluids, and it is possible that it is formed from glucose, together with mannite ($C_{12}H_{12}O_{12} = C_8H_9O_8 + C_4H_2O_3.HO$, Liebig).* This acid is usually obtained by the distillation of amber, to which a little sulphuric acid has been added; the sublimate is then purified by boiling with nitric acid.

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* Handwörterbuch der Chemie, von Liebig, Wöhler, u. Poggendorff. Bd. 3, S. 224.

Tests.—As this acid exhibits no very characteristic reactions towards other bodies, we can only determine its presence by separating it in a state of purity and then analysing it.

Sebacic Acid.—$C_{10}H_8O_3.HO$.

Properties.—This acid (known also as *pyroleic acid*) is, in its external appearance, very similar to benzoic acid, forming white, nacreous, acicular crystals, grouped together in loose heaps: the microscope, however, readily reveals the difference in the external characters of these two acids. It forms either whorled clusters, similar to margaric acid, or large plates extending from a centre, and intersecting one another at various angles, which run into sharp points, without forming an angle capable of measurement; in their mode of grouping, these crystals most closely resemble well-formed crystals of margaric acid; the individual crystalline leaflets are, however, far greater. This acid fuses at 127°, without losing its basic water, into a colourless oil, which, on cooling, solidifies into a crystalline mass; at a higher temperature it sublimes undecomposed; it is only slightly soluble in cold water, but in hot water as well as in alcohol and ether, it dissolves readily; it has a pungent rather than an acid taste, and reddens litmus. By prolonged boiling with nitric acid of 1·4 specific gravity, it is gradually (in six or eight days) converted into pyrotartaric acid. (C. Schlieper.)†

Composition.—According to the above formula it consists of—

Carbon	10 atoms	59·406
Hydrogen	8 „	7·921
Oxygen	3 „	23·762
Water	1 „	8·911
		100·000

The atomic weight of the hypothetical anhydrous acid=

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* Handwörterbuch der Chemie, von Liebig, Wöhler, u. Poggendorff. Bd. 3, S. 124.

† Ann. d. Ch. u. Pharm. Bd. 70, S. 121-129.

1150; its saturating capacity=8·696; its rational formula is $C_8H_8.C_2O_3.HO$.

Combinations.—Its salts are very similar to those of benzoic acid; the alkaline salts are very soluble, the earthy salts are difficult of solution, while those of the oxides of the heavy metals are insoluble.

Pyrotartaric acid, $C_5H_3O_3.HO$, is formed when nitric acid acts on sebacic acid, each atom of the latter assimilating 5 atoms of oxygen, thus $C_{10}H_8O_3+5O=2(C_5H_3O_3.HO)$; it is crystallisable, white, resists the action of the air, fuses at a little above 100°, and sublimes at a higher temperature, developing at the same time a white suffocating vapour; it has a strongly acid taste, dissolves readily in water, alcohol, and ether, and in sulphuric acid without blackening, and expels carbonic acid from its salts; most of its salts are soluble in water and in spirit of wine; with neutral acetate of lead it yields no precipitate, but with the basic acetate, and with nitrate of silver, we have a white, gelatinous deposit which, on drying, becomes brownish white, and translucent. This acid is isomeric, or probably identical, with the *lipic acid* which has been examined by Laurent and Bromeis, and is mentioned in page 74; hence it belongs to the same group of acids as sebacic acid.

Preparation.—This acid is formed during the dry distillation of oleic acid. As it is produced from no other kind of fat, we may determine the presence and amount of olein in a fat, from the presence and amount of the sebacic acid. In order to prepare it, the distillate must be boiled with water as long as crystals continue to be deposited from it on cooling. By a repetition of the crystallisation, the acid may be obtained in a state of purity.

Tests.—In this distillation scarcely any other acid can occur which could be confounded with sebacic acid. It can be distinguished from benzoic acid, to which, as we have observed, it is very similar, by the circumstances that there is a precipitate on the addition of nitrate of silver or of one of the salts of the suboxide of mercury to its hot solution (which is not the case with benzoic acid;) that the sublimed acid crystallises far less readily; that a microscopic examination of the crystals obtained from the aqueous solution, reveals a difference of form; and finally that by the action of nitric acid it is converted into lipic acid.

NON-NITROGENOUS ACIDS.

$$=C_nH_{n-9}O_3.HO.$$

This is also a group of acids which has little relation to animal chemistry, and to which we should make no reference in this place, if it were not that their representative, *benzoic acid*, sometimes occurs in animal fluids, and that its conversion in the animal body has already thrown much light on the metamorphosis of the tissues.

In accordance with the above general formula we have the following acids belonging to this group:—

Benzoic acid	$=C_{14}H_5O_3.HO.$
Myroxylic acid	$=C_{15}H_6O_3.HO.$
Toluylic acid	$=C_{16}H_7O_3.HO.$
Cumic acid	$=C_{20}H_{11}O_3.HO.$
and Copaivic acid	$=C_{40}H_{31}O_3.HO.$

but there are certain other acids, as, for instance, *cinnamic acid*, $C_{18}H_7O_3.HO$, which, partly from their physical properties, and partly on account of the analogy of the products of decomposition, must be regarded as homologous to these acids, although the ratio of the carbon to the hydrogen is not in accordance with the above formula. Moreover, we are acquainted with certain higher stages of oxidation of the same radical, to which stages we assign specific names, and which are impressed with the general character of this group. They contain 5 atoms of oxygen, and are—

Salicylic acid	$C_{14}H_5O_5.HO$	corresponding to	Benzoic acid
Anisic acid	$C_{16}H_7O_5.HO$	„	Toluylic acid
Cumaric acid	$C_{18}H_7O_5.HO$	„	Cinnamic acid
and Copalic acid	$C_{40}H_{31}O_5.HO$	„	Copaivic acid.

All these acids have the following properties in common; they are solid, crystallise readily in needles or scales, are devoid of odour when pure, are fusible, sublime without decomposition, and are slightly soluble in cold water; they dissolve freely in hot water, and crystallise as the solution cools; they are readily soluble in alcohol and ether, and they redden litmus. Their salts present the same analogies.

Physiology itself shows us that cinnamic acid, although not constituted in accordance with the above formula, should be included in this group, for Marchand* has experimentally proved that cinnamic acid, like benzoic acid, is converted in the animal body into hippuric acid.

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* Journ. f. pr. Ch. Bd. 18, S. 35.

Hypotheses of the most varied kinds, chiefly grounded on the products of decomposition, have been set up regarding the rational constitution of these acids. These hypotheses are, however, for the most part limited to the constitution of benzoic acid, and as but few of them are applicable to the other members of this group, we may regard this as an evidence of their untenability. This is partially the case with the hypothesis of Fehling, who, previously to Kolbe, regarded benzoic acid as a conjugated oxalic acid, whose adjunct was phenyl, $C_{12}H_5$. Hitherto, however, the evidence in favour of any one of these hypotheses has not been sufficiently preponderating to warrant its unconditional acceptance.

All these bodies present an analogy in their relations of combination and decomposition. Thus each of these acids presents a series of lower stages of oxidation not dissimilar to the aldehydes of the first group, and containing 1 atom of hydrogen more and 1 atom of oxygen less than the corresponding acid in the anhydrous state. These lower oxides are sometimes acid, sometimes basic, sometimes indifferent volatile oils, some of which occur pre-formed in the vegetable kingdom.

Volatile oil of bitter almonds	$C_{14}H_6O_2$	corresponds with	benzoic acid	$C_{14}H_5O_3$
Salicylous acid	$C_{14}H_6O_4$	„	salicylic acid	$C_{14}H_5O_5$
Hydride of cinnamyl	$C_{18}H_8O_2$	„	cinnamic acid	$C_{18}H_7O_3$
Cumarin	$C_{18}H_8O_4$	„	cumaric acid	$C_{18}H_7O_5$
Cumin	$C_{20}H_{12}O_2$	„	cumic acid	$C_{20}H_{11}O_3$

In all these combinations 1 equivalent of hydrogen may be replaced by 1 equivalent of chlorine, bromine, iodine, or sulphur.

From the chlorine-combinations of this class, we can obtain the corresponding amides by the action of ammonia; thus, for instance, in the case of benzamide, the action is shown by the equation, $C_{14}H_5O_2Cl + H_3N = HCl + H_2N.C_{14}H_5O_2$.

On submitting to dry distillation, the ammonia-salts of the acids containing 3 atoms of oxygen we obtain the corresponding nitriles, which, like the nitriles of the first group of acids, are volatile, inflammable fluids. They are likewise decomposed both by strong acids and alkalies into ammonia and the corresponding acid, and when heated with potassium they yield cyanide of potassium and carbo-hydrogens.

The hydrates of the acids containing 3 atoms of oxygen, when heated with caustic alkalies, lime, or baryta, yield to them 2 atoms of carbonic acid, and become converted into non-oxygenous oils:—

Hydrated benzoic acid	$C_{14}H_6O_4 - 2CO_2 = C_{12}H_6$ =Benzole or Benzin
Hydrated cumic acid	$C_{20}H_{12}O_4 - 2CO_2 = C_{18}H_{12}$=Cumole or Cumin
Hydrated toluylic acid	$C_{16}H_8O_4 - 2CO_2 = C_{14}H_8$ =Toluole or Toluin

In these carbo-hydrogens we may again replace 1 equivalent of hydrogen by 1 equivalent of chlorine, bromine, iodine, or hyponitric acid (HO_4); and in this way there are formed, for instance, chlorobenzide, $C_{12}H_5Cl$, bromocumide, $C_{18}H_{11}Br$, iodotoluide, $C_{14}H_7I$, and nitrobenzide, nitrocumide, and nitrotoluide, $C_{12}H_5.NO_4$,$C_{18}H_{11}.NO_4$ and $C_{14}H_7.NO_4$.

These last-named nitrogenous compounds form yellow, oleaginous bodies, from which, by the action of sulphuretted hydrogen, we obtain the organic, non-oxygenous, volatile bases, benzidine, $C_{12}H_7N$, cumidine, $C_{18}H_{13}N$, and toluidine, $C_{14}H_9N$ (according to the equation $C_{14}H_7.NO_4 + 6HS = 4HO + 6S + C_{14}H_9N$).

BENZOIC ACID.—$C_{14}H_5O_3.HO$.

Chemical Relations.

Properties.—In its sublimed state this acid occurs in colourless, delicate needles; in the moist way it crystallises in scales, or small prisms, or six-sided needles (the primary form of the right rhombic prism); it fuses at a temperature exceeding 120°, boils at 239°, and then becomes converted into a thick, irritating vapour; it is not decomposed either by nitric or by sulphuric acid; in other respects it has the general properties of the acids of this group.

Composition.—In accordance with the above formula, it consists of:—

Carbon	14 atoms	68·853
Hydrogen	5 „	4·098
Oxygen	3 „	19·672
Water	1 „	7·377
		100·000

The atomic weight of the hypothetical anhydrous acid = 1412·5, and its saturating capacity = 7·079.

Combinations.—Most of the benzoates are soluble in water; the alkaline and magnesian salts are very soluble, but do not readily crystallise; the combinations of benzoic acid with the oxides of the heavy metals are for the most part difficult of solution, but are taken up more freely by hot than by cold water.

Products of its metamorphosis.—Oil of bitter almonds is usually regarded as a combination of a hypothetical oxygenous radical (benzoyl) with hydrogen; it is thus a hydride of benzoyle, $C_{14}H_5O_2.H$; it is a thin, colourless liquid whose specific gravity is 1·043 and whose boiling point is 180°; when exposed to the air it oxidises and becomes converted into hydrated benzoic acid. It not only occurs in oil of bitter almonds, but is often found as a product of decomposition when albuminous or gelatinous substances are treated with strong oxidising agents (Guckelberger).* The one equivalent of hydrogen of this body may not only be replaced by chlorine, bromine, or iodine, but also by sulphur or cyanogen.

Benzamide, $H_2N.C_{14}H_5O_2$, whose preparation is noticed in the introductory remarks on this group, is a beautifully crystallisable body which is soluble in water, alcohol, and ether, and possesses all the known properties of the amides.

Benzonitrile, $C_{14}H_5N$, whose formation has also been alluded to, is a colourless oil, which boils at 191°, dissolves in 100 parts of boiling water, and in alcohol and ether in every proportion; as, when treated with potassium, it yields cyanide of potassium, many regard it as cyanide of phenyl, $C_{12}H_5.C_2N$.

If azobenzide, $C_{12}H_4N$, be dissolved in alcohol, the solution saturated with ammonia, and sulphuretted hydrogen passed throughout, we obtain the organic base, *benzidine*, $C_{12}H_6N$.

Benzoin, $C_{14}H_6O_2$, (isomeric with oil of bitter almonds) is formed by the contact-action of the caustic alkalies on oil of bitter almonds containing hydrocyanic acid; it occurs in prisms which are devoid of colour, taste, and smell, and which may be sublimed without undergoing decomposition; it dissolves in concentrated sulphuric acid, and in an alcoholic solution of caustic potash, communicating in each case a blue tint to the mixture; on passing its vapour through a red hot tube it is again converted into oil of bitter almonds. By the action of chlorine it loses 1 equiv. of hydrogen, and is converted into *benzile*, $C_{14}H_5O_2$, which is isomeric with the hypothetical radical, benzoyl, crystallises in sulphur-yellow six-sided prisms, and is fusible and capable of sublimation.

Benzine or *benzol*, $C_{12}H_6$, is obtained, as has been already mentioned, on treating benzoic acid with an excess of hydrated lime; it is a colourless inflammable fluid with an ethereal odour, is solid at 0°, boils at 86°, is insoluble in water, but dissolves in alcohol and ether. Amongst the many other substances which have been obtained from benzine, we may mention *nitrobenzide*, $C_{12}H_5NO_4$, a yellow fluid with a sweetish taste and a cinnamon-like odour, which is not decomposed by the alkalies. If an alcoholic solution of this nitrobenzide be treated with hydrated potash and then distilled, there is produced a non-oxygenous, nitrogenous body, *azobenzide*, $C_{12}H_4N$, forming large, red, fusible, and volatile crystals, which neither corresponds with the nitriles nor possesses basic properties like the organic, non-oxygenous bases.

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* Ann. d. Ch. u. Pharm. Bd. 64, S. 46 ff.

Preparation.—Benzoic acid is found in many of the resins or balsams, but occurs in the largest quantity in the resin known as gum-benzoin, from which it is ordinarily prepared either by sublimation, or, in the moist way, by dissolving the resin in spirit of wine, adding an aqueous solution of carbonate of soda, and then precipitating the benzoic acid by the addition of hydrochloric acid to the filtered and concentrated fluid.

Tests.—Benzoic acid is less to be distinguished from other substances by its volatility, than by its property of separating in crystalline scales from very concentrated aqueous solutions on the addition of an acid. But in carrying on investigations in relation to benzoic acid we must be especially careful respecting the evaporation of the fluid, since it volatilises very readily with the steam; we may easily perceive delicate crystals on the paper covering of the evaporating basin, when acid fluids of this nature have been evaporated without due care; it is therefore better not to add an acid to the fluid till after evaporation, or if it be already acid, to render it alkaline previously to evaporating it. I have found the following method applicable to the discovery of small quantities of benzoic acid in the animal fluids: the alcoholic extract of the fluid in question (for the alkaline benzoates and benzoate of lime are soluble in alcohol) must be mixed with a little acetic, hydrochloric, or lactic acid; if distinct crystals of benzoic acid do not now separate, the mass must be extracted with ether, and the ethereal solution submitted to spontaneous evaporation; from this ethereal extract, which is usually of an oily fluid character, the benzoic acid separates in a crystalline form on the addition of water. When too much fat is present, we must treat the separated mass with dilute spirit, which dissolves the benzoic acid without acting on the fat; on the evaporation of this spirituous solution, we obtain the benzoic acid in a tolerably pure crystalline state, mixed with other free but fluid acids. Under the microscope it appears in rectangular tablets, which, for the most part, are arrayed in rows, being linked together by their opposite angles. Its slight solubility in water, the facility with which it sublimes (as may be seen with a minute quantity between two pieces of flat glass or shallow watch-glasses), together with its crystalline form, afford strong presumption of its presence. Since the remaining acids of this group, which in other respects are very similar to benzoic acid, are not found in the animal body, they cannot give rise to any confusion or mistake in testing for this acid. We have already explained in p. 77, how it may be distinguished from succinic acid, and from sebacic acid, which, however, can scarcely be regarded as existing preformed in the animal body. The mode of distinguishing it from hippuric acid, which closely resembles it in physical properties, will be given in a future page. If we can obtain a sufficient quantity, an elementary analysis and a determination of the atomic weight are by no means superfluous.

Physiological Relations.

Occurrence. In a physiological point of view, benzoic acid deserves a full consideration, although numerous experiments render it probable that it does not exist preformed in any animal fluid. No one has suspected its presence in any animal fluid but the urine; and in this, both in the case of herbivora and carnivora, it occurs very often in the place of hippuric acid. Liebig*, in his classical essay on Fermentation, Putrefaction, and Decay, attributed the occasional occurrence of benzoic acid, in place of hippuric acid, in the urine of horses, solely to a process of fermentation which the latter acid underwent when the urine began to decompose; benzoic acid being formed from it, together with other products. Subsequently,† however, he changed his opinion, believing that he had ascertained that horses, when very hardly worked, and living on insufficient fodder, discharged urine containing benzoic acid, while, under the opposite conditions, the urine contained hippuric acid. In order to ascertain which, or whether either of these views were correct, I‡ analysed the urine of a large number of horses, both well-fed and half-starved, and healthy and diseased; but invariably found hippuric acid and no benzoic acid, unless when the urine had been a good deal exposed to the air at an ordinary temperature. But, on the other hand, when it had stood for some time in the stable, and began to be ammoniacal, it never contained hippuric acid, but only benzoic acid. Hence, too, it is that we so often meet with only benzoic acid in human urine, which, as it contains a far smaller proportion of hippuric acid, must be employed in larger quantities; and if some portions of it have been long exposed to the air, which can hardly be avoided, they produce such a change that only benzoic acid is found in the whole urine. Hence it appears to be the fact, as Liebig assumed, that a ferment is formed in the urine through which the nitrogenous hippuric acid is converted into benzoic acid; for if we mix a specimen of urine containing benzoic acid, whether from man or from the horse, with another specimen containing hippuric acid, on separating the acids from the mixture we almost constantly obtain benzoic acid alone, the ferment of the urine containing benzoic acid probably acting on the hippuric acid of the fresh urine even during the evaporation of the mixture. Moreover, the conversion of benzoic acid conveyed into the organism, into hippuric acid, which was invariably observed by Wöhler and Keller*, Ure,† and subsequent experimenters, is in accordance with the idea that the former, when it occurs in the urine, is only a product of decomposition of the latter.

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* Ann. d. Ch. u. Pharm. Bd. 30, S. 261 ff.

† Ibid. Bd. 41, S. 272.

‡ Handwörterbuch d. Physiol. Bd. 2, S. 14.

Action. We shall return to the behaviour of benzoic acid in the living animal body when we treat of hippuric acid. We will here only remark that the ingestion of this acid causes an extremely disagreeable irritation in the throat, and subsequently a very profuse diaphoresis; and, finally, that it is one of the very few acids which produce a marked augmentation of the acidity of the urine.

NON-NITROGENOUS ACIDS.

$$=C_nH_{n-1}O_5.HO.$$

We make a special group of these acids, although their sole representative is lactic acid. Although this acid deserves a special chapter in every work on physiological chemistry, we see good reason for classing it in a special group of acid bodies. We have already remarked (see p. 56) that in its composition lactic acid presents a close analogy to metacetonic acid; it is more than probable that many other acids exist which stand in the same relation to the individual members of the first-described group of acids, as lactic acid stands to metacetonic acid; and, in point of fact, Cahours,* and subsequently Strecker,† arrived at the discovery of some such acids by a perfectly different train of ideas from that which we have pursued. The latter, in employing Piria's method of decomposing the amide compounds, (given in p. 36,) with the view of ascertaining whether certain nitrogenous animal substances were amides, found two such acids constituted according to the above general formula. In treating glycine with nitrous acid, he discovered an acid$=C_4H_3O_5.HO$, corresponding to acetic acid, and on treating leucine in a similar manner, he obtained an acid $=C_{12}H_{11}O_5.HO$, analogous to caproic acid.

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* Ann. d. Ch. u. Pharm. Bd. 43, S. 108.

† Medico-Chirurgical Transactions. Vol. 24, p. 30

Acetic acid	$C_4H_3O_3.HO$	corresponds to	glycic acid	$C_4H_3O_5.HO$
Metacetonic acid	$C_6H_5O_3.HO$	"	lactic acid	$C_6H_5O_5.HO$
Caproic acid ...	$C_{12}H_{11}O_3.HO$	"	leucic acid	$C_{12}H_{11}O_5.HO$

In the decomposition of hippuric acid, according to the same method, Strecker obtained a new acid, whose composition is not in accordance with the above formula, but is very similar to that of lactic acid: it is represented by the formula $C_{18}H_7O_7.HO$; hence it is analogous in its constitution to the neutral carbo-hydrates of the vegetable kingdom (starch, sugar, woody fibre); that is to say, in addition to carbon it contains hydrogen and oxygen in the exact proportions to form water. Here, too, we should place the cholesteric acid$=C_8H_4O_4.HO$, discovered by Redtenbacher, which also presents much similarity in its characters with the above-named acids of the carbo-hydrates.

There is little to be said regarding the general properties of the acids of this group, as in truth, lactic acid is the only one of them with whose characteristics we are accurately acquainted. It appears, however, from Strecker's communications, that all these acids, when deprived as much as possible of water, occur as oily, non-crystallisable fluids, redden litmus strongly, undergo decomposition when heated, and form soluble and in part crystallisable compounds with bases.

LACTIC ACID.—$C_6H_5O_5.HO$.

Chemical Relations.

Properties.—In its most concentrated state lactic acid is a colourless, inodorous, thick, syrupy fluid, which cannot be solidified by the most intense cold; its specific gravity = 1·215; it dissolves readily in water, alcohol, and ether, attracts water from the atmosphere, has a strongly acid taste and reaction, decomposes when heated, and displaces not only volatile acids but even many of the stronger mineral acids from their salts. Heated with concentrated sulphuric acid, it yields almost pure carbonic oxide gas, and is converted into a substance resembling humin; it gives, however, no trace of formic acid.

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* Compt. rend. T. 27, p. 267.

† Ann. d. Ch. u. Pharm. Bd. 68, S. 52-55.

Composition.—According to the above formula it consists of:

Carbon	6 atoms	40·000
Hydrogen	5 „	5·555
Oxygen	5 „	44·445
Water	1 „	10·000
		100·000

The atomic weight of the hypothetical anhydrous acid = 1012·5, and its saturating capacity = 9·876.

Combinations.—With bases lactic acid generally forms neutral salts, all of which are soluble in water, and many in alcohol, but none in ether. Most of the lactates may be heated to 150° or 170°, and some even to 210°, without undergoing decomposition. The alkaline lactates are not crystallisable, and by the greatest concentration can only be reduced to syrupy fluids; and the same is the case with the lactates of baryta, alumina, sesquioxide of iron, and binoxide of tin; but all other lactates crystallise with tolerable facility, and are capable of resisting the action of the atmosphere. The following peculiar relation has recently been observed in the crystallisable lactates; the lactic acid obtained from animal fluids, and that produced by the fermentation of sugar, form, with the same base, salts which present certain differences in the amount of their water of crystallisation, in their degree of solubility, and in their decomposition by heat, (Liebig,[*] Engelhardt and Maddrell,[†] Engelhardt[‡]). This is, however, a subject requiring further investigation; at least Liebig thinks that he has obtained from the acid of *Sauer-kraut* a zinc-salt which corresponds with that yielded by the muscular juice; and in my own researches, whenever I have analysed the lactic acid of the gastric juice in combination with magnesia or zinc, I have always found it corresponding with that obtained from sugar. Engelhardt distinguishes the acid obtained from muscular juice as *a* lactic acid, and that produced bythe fermentation of sugar as *b* lactic acid.

Lactate of lime, $CaO, a\,\overline{La} + 4HO$, $CaO.b\,\overline{La} + 5HO$, occurs in the form of white hard bodies, which under the microscope are seen crystallising in tufts of delicate needles, each two of which are so placed in relation to the other, that collectively they resemble overlapping tufts or pencils: their form is tolerably characteristic, and they cannot be confounded with other organic lime-salts, as for instance, the butyrate. Lactate of lime loses all its water at 100°, and is soluble in almost every proportion in boiling water and in alcohol; the salt of the *a* lactic acid dissolves, however, in 12·4 parts of water, and that of the *b* lactic acid in 9·5 parts; both salts may be heated to 180° without decomposition.

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[*] Ann. d. Ch. u. Pharm. Bd. 62, S. 312.

[†] Ibid. Bd. 63, S. 83-120.

[‡] Ibid. Bd. 65, S. 359-366.

A crystallographic investigation shows that the *b* lactates of magnesia, of protoxide of manganese (which is colourless or of a pale amethystine tint,) of protoxide of iron (which is of a pale yellow colour), of cobalt (which is of a peach-colour), of nickel, and of zinc, are isomorphous, since with three atoms of water of crystallisation, they form vertical prisms with horizontal terminal surfaces, or with superimposed obtuse horizontal prisms.

Lactate of magnesia.—The salt of *a* lactic acid contains 4 atoms of water of crystallisation, and is somewhat more soluble in spirit than that of *b* lactic acid.

Lactate of nickel is of an apple-green tint, and is difficult of solution in cold water and in spirit; the salt of *a* lactic acid loses all three of its atoms of water at 100°, while that of *b* lactic acid does not part with its third atom at a lower temperature than 130°.

Lactate of zinc.—The *a* lactate of zinc contains only 2 atoms of water of crystallisation, which it very slowly loses at a temperature of 100°; it begins to decompose at 150°, is soluble in 5·7 parts of cold and 2·88 of hot water, and in 2·23 parts of alcohol; the *b* lactate loses its water of crystallisation very rapidly at 100°, bears exposure to a temperature of 210° without decomposition, and dissolves in 58 parts of cold and 6 of boiling water, but is almost insoluble in alcohol. C. Schmidt,* who is the only observer who has devoted great attention to the forms of microscopic crystals with the object of diagnosing such bodies in the animal fluids, gives a very accurate description and figure of the form of lactate of zinc; he mentions the club-like shape of the crystals during their process of formation, and their curved surfaces, as especially characteristic of this salt.

Lactate of cadmium crystallises in anhydrous needles, and is almost insoluble in alcohol.

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* Entwurf e. allg. Untersuchungsmeth. der Säfte u. Excr. 1846, S. 78 ff.

Lactate of copper formed with the *a* lactic acid crystallises in hard, light blue, warty masses, dissolves in 1·95 parts of cold and 1·24 of hot water, and very readily in alcohol; at 100° it begins slowly to lose a portion of its water, and at 140° it decomposes, with a separation of suboxide of copper. Lactate of copper formed with the *b* lactic acid, with 2 atoms of water of crystallisation, occurs in much larger crystals of a dark blue or green tint; it dissolves in 6 parts of cold and 2·2 of boiling water, in 115 parts of cold and 26 of boiling alcohol; it parts with its water very readily and perfectly, both at 100°, and *in vacuo*, and does not become decomposed at a temperature lower than 200°, when it inflames and smoulders.

Basic lactate of protoxide of tin, $2SnO. \overline{La}$, is a crystalline, anhydrous powder, which is very insoluble in water, and absolutely so in alcohol.

Lactate of suboxide of mercury, $Hg_2O. \overline{La}+2HO$, forms red crystals which are difficult of solution, and which, on boiling, become decomposed into a salt of the oxide, and into metallic mercury.

Basic lactate of protoxide of mercury, $2\,HgO.\overline{La}$, forms anhydrous glistening prisms, difficult of solution.

Lactate of silver, $AgO. \overline{La}+2HO$, occurs in needles of a silky, glistening appearance, which blacken when exposed to light. This salt is almost insoluble in cold, but dissolves very readily in hot alcohol; it decomposes at 100°; the aqueous solution, when boiled gradually, assumes a blue tint and deposits brown flocculi.

Products of its metamorphosis.—Lactide, $C_6H_4O_4$. On heating the ordinary, colourless, hydrated lactic acid to 130°, water and a little lactic acid distil over, whilst there remains a yellowish white solid substance, which is very fusible, very bitter, almost insoluble in water, but dissolves readily in alcohol and ether, and whose composition is expressed by the formula, $C_6H_5O_5$. This product, when boiled with water, or for a long time exposed to the atmosphere, becomes again converted into ordinary hydrated lactic acid, and with milk of lime it yields the ordinary lactate of lime (Pelouze*.) If, however, either this so-called anhydrous acid or the hydrated lactic acid be heated to 250°, the products of decomposition are carbonic acid, carbonic oxide, lactide and lactone, but no carbohydrogen. The lactide occurs as a sublimate which must be purified by solution in boiling alcohol. It crystallises from this fluid in white tablets which fuse at 107° and volatilise at 250°; the fused crystals solidify on cooling, into a crystalline mass which is devoid of odour, has a slightly acid taste, and dissolves slowly in water; its conversion into lactic acid is more rapid than that of the so-called anhydrous lactic acid.

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* Compt. rend. T. 19, p. 1219-1227.

Lactone, $C_{10}H_8O_4$ (produced according to the formula $2C_6H_5O_5.HO-[2CO_2+4HO]=C_{10}H_8O_4$) is obtained on distilling anew the fluid products of distillation of lactic acid, washing the distillate with water, and drying the insoluble portion with chloride of calcium; the pure lactone is a colourless fluid with an aromatic odour and a burning taste, which boils at 92°, and when inflamed, burns with a blue tint.

Lactamide, $C_6H_7NO_4=H_2N.C_6H_5O_4$, is formed from lactide and dry ammoniacal gas: it crystallises in colourless, right rectangular prisms, and is decomposed into ammonia and lactic acid. This body is moreover isomeric with the powerful base, *sarcosine,* discovered by Liebig, and with the longer-known indifferent substance, *urethran.*

Preparation.—Lactic acid is very often formed during the fermentation of fluids containing sugar or starch, and it might as well be maintained that there is a specific lactic fermentation, as that there is a distant acetic or butyric fermentation. Hence lactic acid is not only found in milk which is turned sour, but also in the acid waters of starch fabrics, in *Sauer-kraut,* in sour cucumbers, in fermented beet-root juice, &c. (The conditions under which this conversion takes place are explained in a future part of this work under the head of "fermentation of milk.")

The best method of obtaining lactic acid is by exposing sugar to this kind of fermentation, under the combined influence of milk and cheese.

Bensch* has employed the following practical method of obtaining it: 6 parts of cane-sugar, $\frac{1}{16}$th part of tartaric acid, 8 parts of sour milk, $\frac{1}{2}$ part of old cheese, and 3 parts of levigated chalk, are mixed with 26 parts of water, and exposed to a temperature of 32°. In the course of eight or ten days a semi-solid magma of lactate of lime is formed; on boiling it with 20 parts of water and $\frac{1}{16}$th part of caustic lime, filtering it at a boiling temperature, and slightly evaporating it, the lactate of lime separates in a few days in granules. The salt must be drained and pressed, again dissolved in twice its weight of water, decomposed with $\frac{7}{32}$ parts of sulphuric acid, the precipitated gypsum removed by filtration, and the acid fluid saturated with $\frac{3}{16}$ of carbonate of zinc. The crystallised zinc-salt must then be decomposed by sulphuretted hydrogen, and the fluid concentrated, first by warmth, and afterwards *in vacuo:* the hydrated lactic acid is finally obtained in a state of purity by solution in ether.

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* Ann. d. Ch. u. Pharm. Bd. 61, S. 174-176.

Liebig* prepares lactic acid from the juice of flesh, in the following manner. Flesh from which the fat has been most carefully removed, is very finely chopped, repeatedly kneaded with water, and exposed to strong pressure; the fluid thus obtained is heated till it boils, filtered to remove the coagulated matters, decomposed with baryta-water, again filtered, and very strongly concentrated by evaporation. In the course of a few days the creatin crystallises; the milky liquid poured away from these crystals is rather more strongly concentrated; and then gradually treated with small portions of alcohol, which causes the crystallisation of the inosinates of baryta and potash. The mother-liquid, after the separation of the inosinates, is evaporated, and the residue extracted with alcohol; after this alcoholic extract has stood for a considerable time crystals are formed from it, while nearly pure lactate of potash remains in the mother-liquid. To this we must add sulphuric acid or a solution of oxalic acid (containing one-third of the acid), and then precipitate the sulphate or oxalate of potash by means of alcohol. The fluid filtered from the potash-salt is treated with ether, as long as any precipitation continues; the solution is then evaporated to a syrup, and treated with half its volume of spirit and five times its volume of ether, which takes up nearly pure lactic acid.

From this we may prepare lactate of lime, whose spirituous solution must be purified by animal charcoal, and evaporated, so that the salt may crystallise; the lactic acid is then readily separated from the lime-salt by sulphuric or oxalic acid with the aid of alcohol and ether.

Tests.—To determine the presence of lactic acid is one of the most difficult tasks in analytical animal chemistry, as is indeed evinced by the prolonged contest that existed regarding the presence or absence of this acid in the animal organism. In order to determine its presence with certainty, it must in the first place be separated from all other organic substances, but in this lies one of the great difficulties; for there is scarcely any other acid to which foreign bodies adhere so tenaciously. Liebig's method (which we have given) of preparing lactic acid from muscular juice is one of the best means of separating this acid from animal fluids. If we are sufficiently acquainted with the properties of lactic acid and its salts, we may modify this method in many respects, which is indeed the more necessary, since, in investigations relating to animal chemistry, we rarely have so large a quantity of material to work upon as is required in accurately following the steps laid down by Liebig. From most of the other animal fluids we can rarely obtain a sufficient quantity of lactic acid to serve for an elementary analysis. Indeed it often happens that we cannot even obtain enough of a *pure* lactate to enable us to determine the atomic weight. Hence, it is very often necessary to found our decision regarding the presence of lactic acid almost entirely on the crystalline form of its salts. Although many of the other properties of the lactates may contribute to establish the proof of the presence of this acid, yet a crystallometric investigation, made with the aid of the microscope, can alone be regarded as approximating in certainty to an elementary analysis.

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* Ann. d. Ch. u. Pharm. Bd. 62, S. 312.

In consequence of the extremely minute quantity of lactic acid to be obtained from the animal fluids, I am in the habit of adopting the following method, which may be readily modified in particular cases, with the view of studying the forms of the different salts under the microscope. The impure lactic acid prepared from the alcoholic extract by sulphuric or oxalic acid is treated with baryta-water, and the excess of the baryta removed by carbonic acid; the solution of lactate of baryta is evaporated to the consistence of a syrup, treated with alcohol, filtered, again evaporated, and then allowed to stand for some time, in order that the other baryta-salts, (for instance, the butyrate and inosinate) may crystallise; the syrup is then allowed to trickle away, or if it be not withdrawn, is dissolved in water and decomposed with a solution of gypsum; the fluid from which the sulphate of baryta has been removed by filtration is strongly concentrated, and on examining it under the microscope we can readily perceive the double brushes of lactate of lime which we have already described, in addition to crystals of gypsum. On dissolving these crystals of lactate of lime in alcohol, and adding sulphate of copper to the alcoholic solution, the fluid, after standing for some time (in order that the excess of of sulphate of copper and the gypsum that is formed may separate as completely as possible) is evaporated so as to crystallise, and the crystals of lactate of copper are then microscopically examined. If, by the above process, we do not succeed in obtaining distinct and measurable crystals, we must dissolve the residue in a little water; and (in order to decompose or separate any butyric acid that may be present) we must boil it strongly, filter it, and, after concentrating it, place on it a small zinc bar. Since, as we have already mentioned, lactate of copper is far more soluble in water than lactate of zinc, the zinc very soon becomes covered with white crystals of lactate of zinc, if the fluid be sufficiently concentrated, and these crystals, if they be allowed to remain for some time, may usually be easily measured under the microscope. Distinct crystalline forms may even be distinguished with the naked eye. If, however, in consequence of the want of a Goniometer, an accurate crystallometric investigation cannot be instituted, we must precipitate the solution of the zinc-salt with a boiling solution of protochloride of tin, and allow it to stand for some time; on then making a microscopic examination, we shall find clusters of crystals whose groups are composed of thick rhombic tablets lying close upon one another. When we have in this way prepared and explored the different lactates, (and after some practice, tolerably small quantities are sufficient for this purpose,) we hardly require to make an elementary analysis or to determine the atomic weight, to enable us to decide regarding the presence of lactic acid.

Physiological Relations.

Occurrence.—The doubts regarding the nature of the free acid of the *gastric juice* have given rise to a great number of investigations on this point. Prout* and Braconnot† believed that their experiments showed that the gastric juice contained no lactic acid, but only hydrochloric acid. Subsequently, I thought that I had satisfactorily proved‡ the existence of lactic acid in the gastric juice of various carnivorous and herbivorous animals, by obtaining from it several of the lactates, and referred the occurrence of free hydrochloric acid simply to the decomposition of the metallic chlorides by the lactic acid during the evaporation or distillation of the gastric juice. Hünefeld § supported this view. A period now arrived when Liebig totally denied that lactic acid occurred in any of the animal fluids, and, consequently, in examining the gastric juice of a criminal immediately after he had been beheaded, Enderlin || was just as unable to detect lactic acid, as he has been to find carbonate of soda in the blood-ash. Blondlot,¶ also, in examining pure gastric

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* Phil. Trans. for 1824, p. 45.

† Ann. de Chim. T. 59, p. 348.

‡ First edition of this work, 1840. Bd. 1, S. 284. Bericht über d. Fortschritte der physiol. u. path. Ch. im J. 1842. Leipzig. S. 10.

§ Chemie u. Medicin. Bd. 2, S. 81 ff.

|| Ann. d. Ch. u. Pharm. Bd. 46, S. 123.

¶ Traité analytique de la Digestion. Paris et Nancy. 1843. p. 244.

juice from dogs, found no lactic acid, and ascribed the acid reaction of the fluid to acid phosphate of lime, while Lassaigne,* in opposition to this view, attempted to prove the presence of free hydrochloric acid. Subsequently, experiments have been instituted by Bernard and Barreswil,† Pelouze,‡ and Thomson,§ which have led all these chemists to believe that they have proved the existence of lactic acid in pure gastric juice. Very recently I ‖ prepared the lactates from a larger amount of pure gastric juice than had hitherto been employed, and obtained them in such quantities that I was enabled to make an ultimate analysis of several of them, and to determine the atomic weight, which proved that the acid of the gastric juice is perfectly identical with lactic acid. I found that pure gastric juice, even on mere evaporation *in vacuo*, undoubtedly developes hydrochloric acid (in one case it amounted to 0·125%), but that there is then always an acid residue left, which, besides free lactic acid, contains lactate of lime and alkaline chlorides; whence we may conclude that there are in the gastric juice both free lactic acid and lactates, in addition to free hydrochloric acid.

According to my observations, chloride of calcium, but not chloride of sodium, (as Bernard and Barreswil maintain,) is decomposed during evaporation with free lactic acid, even *in vacuo;* hence it is not surprising that pure gastric juice should develope vapours *in vacuo*, which, when passed into a solution of nitrate of silver, should form chloride of silver. I must further remark, that the lactates obtained from the pure gastric juice, as well as from the contents of the stomach, had not the composition of the *a* lactic acid, but that of the *b* lactic acid obtained from sugar. Bernard and Barreswil allege, in opposition to Prout's opinion, that pure gastric juice is rendered decidedly turbid by a drop of a dilute solution of oxalic acid, while an equal quantity of oxalic acid in a solution of lime containing only $\frac{1}{1000}$th part of free hydrochloric acid, causes no precipitate. Further, starch, when boiled with hydrochloric acid, loses its property of being coloured blue by iodine, while lactic acid does not induce this change. On boiling a solution of a lactate with a little hydrochloric acid and starch, the properties of the last-named body remain unaffected: starch boiled with gastric juice retains the property of being coloured blue by iodine.

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* Journ. de Chim. méd. T. 10, p. 73 et 189.

† Journ de Pharm. et de Chim. Janv. 1835. p. 49.

‡ Compt. rend. T. 19, p. 1227.

§ Philos. Mag. 3rd series. Vol. 26, p. 420.

‖ Berichte d. Gesellschaft d. Wiss. zu Leipz. Bd. I, S. 100-105.

Various authors have assumed that alkaline lactates are present in normal *saliva*, and have referred the acid reaction which is occasionally noticed in that fluid to the presence of free lactic acid, but in the small amount of solid residue which is left by the saliva, I have never been able to establish with certainty the presence of lactates, even when operating on considerable quantities (obtained both from man and from the horse); I had, however, an opportunity of collecting large quantities of the saliva of a patient labouring under Diabetes mellitus, and in this case I convinced myself beyond all doubt of the presence of free lactic acid.

In all the cases of Diabetes mellitus which I have observed, the saliva has had an acid reaction: associated with this symptom and with intense thirst, we sometimes find a copious secretion of saliva, which we have thus a good opportunity of analysing. As the saliva of such patients sometimes (but not always) contains sugar, I took care that it should flow directly from the mouth into alcohol, so as to avoid any possible formation of lactic acid from the sugar. The zinc-salt which was obtained, showed very distinctly the crystalline form of the lactate.

Notwithstanding the assumed neutralising property of the bile, the contents of the small intestines of herbivorous, carnivorous, and omnivorous animals, always exhibit an acid reaction, which, however, diminishes towards the ileum; the acid reaction is strongest in the duodenum, especially in herbivorous animals. That the acid reaction here depends on the presence of lactic acid, may be most readily shown in the horse, in whose duodenum we find lactate of lime and free lactic acid, especially after the ingestion of amylaceous food.

Whether the acid reaction of the mucous secretion of fasting animals depends on lactic acid, cannot with certainty be decided, in consequence of the small quantities in which it can be collected.

I have repeatedly allowed the contents of the duodenum of a recently killed horse (healthy, and killed either in consequence of an accident or from its being affected with malleus) to flow directly into alcohol, and after filtering the fluid while hot, and concentrating it, I have obtained a white granular sediment, which, under the microscope, exhibited the well-known double-brush form of lactate of lime: a quantity collected for analysis contained 28·97% of water, and in the anhydrous state, 25·831% of lime, 32·982% of carbon, and 4·513% of hydrogen; this salt was therefore *b* lactate of lime. The lactic acid was separated in the ordinary manner from the alcoholic solution, and the magnesian and zinc salts were crystallometrically examined and quantitatively analysed, so that there can be no doubt regarding the existence of lactic acid in this fluid.

Tiedemann and Gmelin*, and Valentin†, attribute the acid reaction of the mucus of the small intestines to lactic acid, because this mucus, on incineration, yields an ash abounding in carbonates, which, at all events, could not be the case to such a degree, if the free acid of this mucus were a mineral acid.

Moreover, the contents of the large intestine have often an acid reaction, and indeed constantly after the use of vegetable food: in two cases in which I was able to collect large quantities of these contents from a preternatural anus in the ascending colon, I obtained quite sufficient lactic acid to test crystallometrically the zinc and magnesian salts.

The fluid secreted by the large intestine (and indeed by the lower portion of the ileum) has always an alkaline reaction; hence the outer parts of the contents of the large intestine are for the most part neutral or alkaline; after the use of vegetable food the inner portion is, however, always acid, as was ascertained by Steinhäuser.‡

Whether lactates constantly occur in the *chyle* must for the present remain undecided. In the chyle obtained in two cases from the thoracic duct of the horse (one horse having been fed with oats two hours before he was killed, and the other with starch-balls), lactic acid was recognised with certainty.

Here, as well as in the investigation of the alcoholic extract of lymph or blood, we must be careful in reference to the salts of the fatty acids; and, consequently, after the separation of the pure lactic acid by ether, the extract should be boiled with water to remove the non-volatile fatty acids, and the solution, when cooled, should be filtered; the lactic acid should then, in the manner we have already described, be transferred to baryta, from this to oxide of copper, and from the latter to oxide of zinc, so as to separate as much as possible the volatile fatty acids. This investigation leaves no doubt regarding the existence of lactates in the chyle of horses during the digestion of amylaceous food.

No one has yet definitely established the presence of lactic acid in the *lymph*, although its presence in the fluid is by no means improbable; since, independently of the circumstance that Marchand and Colberg,[*] as well as Geiger and Schlossberger,[†] found much carbonated alkali in the ash afforded by lymph, whose albuminous constituents were removed previously to incineration, and whose reaction was scarcely, or not at all, alkaline, we cannot readily perceive in what other way than through the lymph the large quantities of the lactic acid formed in the muscles can be carried away.

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* Verdauung. Bd. 1, S. 349.

† Lehrb. d. Physiol. d. Menschen. Bd. 1, S. 343.

‡ Experimenta nonnulla de sensibilitate et functionibus intestini crassi. Diss. inaug. Lips. 1842.

The recognition of lactates in healthy *blood* is just as difficult or impossible as that of urea in the same fluid. It is probable that we shall never obtain a positive demonstration of the existence of alkaline lactates in healthy blood by direct experiment, but the simplest induction proves that they must be present there, even if they only remain in it for a very short period. We know from numerous experiments how rapidly effete matters, and especially salts of easy solubility, are removed from the animal organism by the kidneys; we know with what extreme rapidity iodide of potassium appears in the urine after it has been swallowed; and we know that it is only on that account that urea has not yet been detected in healthy blood, (notwithstanding the assertions of certain persons), for its sojourn in the blood is so very short that the quantity occuring in that fluid at the same time is scarcely to be recognised with our present chemical appliances. (Marchand[‡]). Hence it is not surprising that the presence of lactic acid has never yet been demonstrated, with all the necessary scientific accuracy, in normal blood, especially when we consider that it is removed from the circulating fluid in more ways than one. The combustion of the alkaline lactates—that is to say, their conversion into alkaline carbonates—exceeds in rapidity and extent their passage into the urine. Until we can prove that the lactic acid, which is accumulated in large quantity in the muscular tissue, and is found in the chyle and in the lymph, undergoes decomposition on the spot, we must assume that it passes into the blood, and the more so because we well know that chemical analysis has not yet attained such a degree of accuracy as to enable us to demonstrate the presence of lactic acid in the blood with due scientific precision. In what other way than through the blood could the lactic acid of the chyle or the muscular fibre pass into the urine? Lactic acid, like urea, may collect abnormally in such quantities in the blood as to be capable of detection by chemical analysis. Scherer* has paid especial attention to the occurrence of lactic acid in morbid blood; he observed that, during an epidemic of puerperal fever, the blood had often an acid reaction, and, as this fluid frequently contained only free albumen and no albuminate of soda, it was clear that it must contain a free acid. Scherer certainly did not demonstrate the actual presence of lactic acid in the blood; but, as he actually separated lactic acid from the exudations which were simultaneously present, and recognised it by the form of its salts, we cannot reject his conclusion that the acid reaction of the blood was also due to lactic acid. I have only thrice observed an acid reaction of the blood, and conditions similar to those described by Scherer, namely, in a case of pyæmia in a man, and in the blood of two women (from six to ten weeks after delivery.) In no case could I obtain sufficient material to demonstrate the lactic acid with certainty.

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[*] Poggend. Ann. Bd. 43, S. 625.

[†] Arch. f. physiol. Med. Bd. 5, S. 394.

[‡] Journ. f. prakt. Ch. Bd. 11, S. 49.

The following experiments,† instituted on myself, exemplify the rapidity with which the lactates in the blood are converted into carbonates. Within thirteen minutes after taking half an ounce of lactate of soda, (calculated as dry,) my urine had an alkaline reaction. Moreover, that the conversion of the alkaline salts of the organic acids into carbonates (as was first proved by Wöhler) does not take place in the *primæ viæ*, but in the blood itself, is proved by direct experiments which I made on dogs, by injecting various quantities of lactate of soda into the jugular vein; after five, and at latest after twelve minutes, the urine exhibited an alkaline reaction.

In opposition to the view that lactates exist in the blood, it has been urged that the ash of blood has not an alkaline reaction, and further, that it contains no alkaline carbonates. We have shown in another part of this work that this observation of Enderlin's has not been made or confirmed by any one who has preceded or succeeded him, (see "Ash of the blood",) but that, on careful incineration, carbonated alkali always occurs in the blood; and even if this were not the case, it would be no evidence against the presence of lactic acid, since, on incinerating the blood, there is a combustion of sulphur and phosphorus sufficient to saturate the alkali previously combined with lactic acid. Further, carbonic acid is expelled from the carbonate by ordinary phosphate of soda, which is thus converted into tribasic phosphate of soda.

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* Untersuchungen zur Pathol. Würzburg. 1843. S. 147-194.

† Jahresber. 1843. S. 10.

In *exudations*—those, namely, after puerperal fever—Scherer* found both free and combined lactic acid, often in very considerable quantity. (In one case there was 0·105% of free lactic acid.) In the exudations in a case of empyema, he found albumen uncombined with soda, from which he concluded that the latter had been abstracted from the former in consequence of the presence of lactic acid.

Lactic acid, which was originally discovered by Scheele in milk, does *not* occur in the healthy *milk* of man and animals: it is only in an abnormal state, or after a strictly animal diet, that milk which reddens litmus and probably contains lactic acid, is secreted. It is only after exposure to the atmosphere that healthy milk acquires an acid reaction, which is dependent on the formation of lactic acid from the sugar of milk by fermentation.

It is now forty-two years since Berzelius† recognised the existence of free lactic acid in the *muscular fluid;* and no one who has repeated the experiments of this most faithful and accurate experimentalist, can confound this acid with any other, since its properties, and those of its salts, have been made known by more recent investigations. Berzelius did not deem it necessary at that time to confirm the proof of the presence of lactic acid in this fluid by an elementary analysis, although he might readily have made one. Liebig, so long as he relied on the investigations of his pupils, absolutely denied the existence of lactic acid in the living animal body; but on instituting and publishing his own admirable inquiry respecting the fluids of the muscular tissue of animals, he could no longer question its presence in the muscular fluid, and even admitted its existence in the gastric juice. Moreover, the free acid exists in so preponderating a quantity in the muscles, that Liebig is of opinion that it is more than sufficient to saturate the alkali of all the alkaline fluids of the animal body. Berzelius thought that he had convinced himself that the amount of free lactic acid in a muscle is proportional to the extent to which it has been previously exercised.

Berzelius separated the lactic acid from the alcoholic extracts of the animal fluids in the following manner. The alkalies having been precipitated by tartaric acid, the filtered acid solution was digested with carbonate of lead; the alcoholic solution of lactate of lead, having been separated from the other lead-salts by filtration, was then treated with sulphuretted hydrogen, which left the lactic

* Op. cit.

† Lehrb. d. Ch. Bd. 9, S. 573; Ann. d. Ch. u. Pharm. Bd. 1, S. 1; Jahresber. Bd. 27, S. 585-594.

acid in solution contaminated merely with extractive matter. After the evaporation of the alcohol the acid was filtered through animal charcoal, from which the earthy salts had been separated, and treated with hydrated oxide of tin, on which the comparatively insoluble lactate of tin was separated. This was again decomposed with sulphuretted hydrogen, and the lactic acid further examined.

Anselmino, Thenard, and Berzelius,* believe that they have found lactic acid and lactate of ammonia in the *sweat*.

Berzelius† also conjectures that alkaline lactates exist in the *bile*.

In consequence of the rapidity with which the alkaline lactates undergo a transformation in the blood, it would naturally follow that lactic acid, when it occurs in the *urine*, would exist there as an extremely variable constituent: and this assumption is confirmed by experience. Earnestly as I formerly maintained the view that lactic acid constantly occurs in animal urine, and that the acid reaction of this fluid is solely dependent on its presence, I have since convinced myself that my earlier modes of analysis, (when I rested satisfied with the mere exhibition of the zinc-salt) though most carefully conducted, were open to deceptions in reference to this acid; but to maintain that the urine of healthy men and animals never contains lactic acid or lactates, under any physiological relations, is to err just as much in the opposite direction. A more extended investigation has led me to the following results. In all cases where the supply of lactates to the blood is very great, —whether this depends on an excess of acid being formed in the muscles, or on the use of a diet tending to produce it, or on an imperfect process of oxidation in the blood,—lactic acid may be detected in the urine with all the certainty which in the present state of chemistry can be expected in such researches. Hence we can understand why it is that, in the urine of the same individual, lactic acid may on one day be present and on another absent;—why, in many persons, no lactic acid can be detected in the urine, and in others again (and especially in those who in consequence of repeated catarrhs suffer from partial relaxation of the pulmonary tissue, and yet often think themselves perfectly well) it is constantly present in the urine;—why stall-fed animals, living on amylaceous fodder, excrete lactic acid by the kidneys (and in part also by the mammary glands,) while under other conditions this acid cannot be discovered in their urine;—and why, finally, in most febrile diseases, lactic acid may be recognised in the urine.

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* Lehrb. d. Ch. Bd. 9, S. 393.

† Ibid. S. 293.

The details of these investigations, which will be given in another place, afford numerous confirmations of the experiments which I formerly instituted on the urine.[*] Berzelius[†], during his later years, entertained no doubt regarding the correctness of the results which he had so long before obtained in reference to the presence of lactic acid in the urine. Boussingault[‡] has quite recently found lactic acid in the urine of pigs fed with potatoes, as well as in that of cows and horses. (In the urine of the horse he found 1·128% of lactate of potash, and 0·881% of lactate of soda.)

In accordance with this view is the almost universal occurrence of lactic acid in urine containing a considerable quantity of oxalate of lime, so that by a microscopic examination of a specimen of urine, a conclusion may often be drawn regarding the presence or absence of lactic acid. Hence in those diseases in which there is an increase in the amount of oxalate of lime, as in pulmonary emphysema, disturbances of the nervous system, rachitis, &c., lactic acid is always associated with this salt. Scherer[§] and Marchand[‖] have sometimes observed a considerable augmentation of lactic acid in the urine in rachitic children, and I have also noticed it in the osteomalacia of adults.

In determining the presence of lactic acid we must always employ fresh urine, if we wish to draw any conclusion regarding the composition of the renal secretion. The admirable investigations of Scherer[¶] regarding urinous fermentation, were the first to direct attention to the circumstance that there is a gradual augmentation of the free acid, when the urine is exposed to the atmosphere. The lactic acid must then be formed from some unknown matter,—probably from what we term an extractive matter. I[**] had formerly observed something similar occur in diabetic urine, since, when freshly passed, I always found it neutral, although subsequently it became acid; in consequence, however, of diabetic urine containing sugar, these experiments were of less weight than those of Scherer. We may hence fairly conclude that the urine, after its excretion from the kidneys, undergoes a similar acidification in the bladder, and consequently that the lactic acid which is often found in the urine discharged from that viscus is a product of decomposition which is formed externally to the sphere of vital activity. If, however, the occurrence of crystals of free uric acid warrants us in inferring the existence of the lactic fermentation, it is only very seldom that it can occur in the bladder, for the cases are extremely rare in which urine on its emission from that organ contains free uric acid; the statement that has found its way into various books, to the effect that fresh urine often contains free uric acid, being a very erroneous one.

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[*] Journ. f. prakt. Ch. Bd. 25, S. 1, and Bd. 27, S. 257; Handwörterb. d. Physiol. Bd. 2, S. 10.

[†] Jahresber. Bd. 27, S. 590.

[‡] Ann. de Chim. et de Phys. 3 Sér. T. 15, p. 97-114.

[§] Untersuchungen z. Pathol. S. 74 ff.

[‖] Lehrbuch d. phys. Ch. S. 105.

[¶] Ann. d. Ch. u. Pharm. Bd. 42, S. 171; and Unters. z. Pathol. S. 1-16.

[**] De urina diabetica. Diss. inaug. Lips. 1835.

C. Schmidt * has separated lactic acid in the form of lactate of zinc, from the strongly acid fluid yielded by the *long bones in a case of osteomalacia.* He measured the angles of the crystals, and submitted the salt to an elementary analysis.

Origin.—If we might be permitted to hazard a conjecture regarding the production of lactic acid from its occurrence in the animal body, we should ascribe to it a double origin. No one can entertain a doubt that the lactic acid, found in the contents of the intestine and in the chyle after the digestion of vegetables, owes its formation to the amylaceous or saccharine matters contained in the food, which in their passage through the *primæ viæ* become converted into that acid, in the same manner as takes place in the fermentation of milk. But the true genesis of the lactic acid which accumulates in such large quantity in the muscles is not so immediately obvious; we may certainly assume that the lactic acid formed in the *primæ viæ* from vegetables is especially attracted by some mechanical or chemical influence of the muscular fibre, and is accumulated there to serve certain definite purposes; but this view is in some measure opposed by the circumstances that the muscles of carnivorous animals contain as much lactic acid as those of herbivorous animals, and that free lactic acid is always found in the urine of carnivora and of men when living on a strictly animal diet, which would scarcely be the case if the acid conveyed to the muscles solely proceeded from the lactic acid contained in the flesh which had been taken as food. But if we regard the lactic acid of the juice of flesh, merely as a product of metamorphosis which is formed while the muscular fibre is discharging its function, (*i.e.* during the contraction of muscle,) the only objection to the view that this acid proceeds from the decomposition of the muscular substance itself, is, that hitherto lactic acid has not been produced either by fermentation or otherwise, from any nitrogenous animal matter, either albuminous or gelatinous. We should, however, not make much progress in our physiological enquiries, if we set down as impossible all the processes which we happen not yet to have recognised external to the living body. Recent investigations respecting the various modes of decomposition and the products of albuminous bodies, show that a partial conversion of albuminous matter into lactic acid is by no means an absurd impossibility; for Guckelberger*, who found aldehyde among the products of oxidation of albuminous bodies, points out that in these substances there must be hidden a group of atoms, from which sugar of milk or lactic acid might be produced. He further proved, experimentally, that sugar of milk with chromic acid also yields aldehyde; and, on the other hand, Engelhardt found aldehyde of acetic acid among the products of distillation of lactate of copper. We have already directed attention to the analogy existing between lactic acid, and that frequent product of the metamorphosis of animal matter, metacetonic acid. Hence it would be not at all surprising, if lactic acid were in some manner obtained from the gelatinous or protein compounds.

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* Ann. d. Ch. u. Pharm. Bd. 61, S. 302-306.

Moreover, this view is supported by the consideration that, besides lactic acid, creatine, which is found in the muscular fluid, is often a product of decomposition of muscular substance, since otherwise it would be found in other places besides the urine. Moreover, according to Liebig's discovery, creatine is decomposed by alkalies into urea and sarcosine, a substance isomeric with lactamide; hence there would be nothing incongruous in assuming that in the natural metamorphosis of creatine in the animal body, where no sarcosine is found, the creatine is still decomposed into urea, but that, in place of sarcosine, there is an abstraction of water, and that lactic acid and ammonia are formed, in which case, however, we should have to explain what becomes of the ammonia. Moreover, it cannot be supposed that lactic acid passes into the muscular substance from the blood, where it is so easily and rapidly consumed; yet such must be the case if it comes from the acid formed in the intestinal canal from amylaceous food.

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* Ann. d. Ch. u. Pharm. Bd. 64, S. 99.

Finally, after the discovery made by Redtenbacher, that glycerine is convertible into metacetonic acid, there seems to be something attractive in the hypothesis that glycerine, which, in the metamorphosis of the fats, obviously undergoes an independent change, is converted into lactic acid, which, as we have already shown, is allied to metacetonic acid. As we have no probable conjectures regarding the further course of the haloid base of the fats in the animal body, it is possible that these substances may contribute, through their base, to the formation of lactic acid.

We have endeavoured, in the above sketch of the occurrence of lactic acid in the animal body, to restrict ourselves most rigidly to established facts, and we have rejected all those of our own experiments on which the slightest doubt appeared to rest: without referring to authorities, we have allowed the facts to speak for themselves, and have attached as little credit to the negative assertions of Liebig, as to the older experiments of Berzelius, regarding the occurrence of lactic acid in bile, sweat, &c., with that impartiality which becomes every one wishing to be an honest scientific observer. We shall now consider the advantages which may accrue to the animal organism from the occurrence of lactic acid in this or that organ, without any reference to the views and errors which we formerly maintained. Although we no longer regard lactic acid as one of the most important elements in relation to the metamorphosis of the animal tissues, it is yet of sufficient importance to attract the attention of physiologists. It is moreover obvious that questions regarding the function of a substance in the animal body, can never receive more than a hypothetical answer; for purposes may indeed be conjectured or understood, but they cannot be palpably demonstrated. If, therefore, we judge of the physiological importance of an animal substance on hypothetical grounds, we do not necessarily adopt lax and untenable illusions of the fancy, but shall confine ourselves to logical conclusions.

Uses.—In ascribing to lactic acid an essential influence on the *digestion* of nitrogenous food, our opinion is based, not on a mere conjecture derived from the constant occurrence of this acid in the gastric juice, but on the result of direct experiments* with artificial digestive fluids, from which it appears that lactic and hydrochloric acids cannot be replaced in the process of digestion, by any other animal or organic acids. The question how the acid acts, will be entered into in our observations on "Digestion."

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* Berichte der Gesellsch. der Wiss. zu Leipzig. 1849.

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* Berichte der Gesellsch. der Wiss. zu Leipzig. 1849.

It is not probable that the lactic acid and lactates found in the *contents of the stomach and intestines*, are entirely derived from the acid of the secreted gastric juice; indeed it is certain that the greater part of the lactic acid, occurring both there and in the chyle, may be traced to the conversion of the starch or sugar of the food; we should, however, on the other hand, be drawing too general a conclusion, if we assumed that all the starch and all the sugar of the food must be converted into lactic acid, in order that the functions of the organism may be duly fulfilled. In the course of our subsequent physiological considerations, we shall explain the grounds why we cannot accept this view, notwithstanding that it is apparently supported by positive observations. This much is, however, supported by facts, that a portion of these substances is actually converted into lactic acid, and passes into the blood in the form of alkaline lactates. If we adopt Liebig's ingenious division of food, into true food for nutrition and food for the respiration, we know of no substitute which could better act in the blood as food for the respiration than the alkaline lactates, which, as we have seen, undergo rapid combustion in the blood, and are thus converted into carbonated alkali,—in a word, nothing could be a better supporter of animal heat than the alkaline lactates.

If the lactic acid in the fluid saturating the *muscles*, although undoubtedly derived from the effete muscular tissue, be not a pure product of decomposition, there is much in favour of Liebig's* hypothesis, that an electric tension influencing the function of the muscles, is established by the acid muscular juice and the alkaline contents of the capillaries.

In the *urine* and *sweat*, lactic acid occurs only as a product of excretion; for even if, in some cases, it may contribute to the solution of the earthy constituents of the urine, its occasional absence in this fluid shows that other substances effecting that object are also present.

I formerly regarded lactic acid as one of the most important agents in the solution and transportation of many of the animal substances and earthy salts of the animal organism; but a more thorough insight into the processes of animal chemistry, has led me almost entirely to renounce this view; for although I† have recently convinced myself that the solvent power which lactic acid exerts over basic phosphate of lime, far exceeds that of acetic acid, and is indeed very considerable—a fact long ago asserted by Berzelius,* and directly proved by the experiments of Gay Lussac,† but whose accuracy has been called in question by Liebig,‡—yet I cannot overlook the circumstance that the albuminous bodies, which are never devoid of phosphate of lime, and often contain a large quantity of it, afford far better means of transport for the bone-earth in the animal body than lactic acid can do.

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* Op. cit.

† Jahresb. der ges. Med. 1843, S. 10.

How far my former view, that lactic acid is the most important factor in the metamorphosis of the animal tissues, can still be maintained, may be seen from the preceding observations.

SOLID FATTY ACIDS.

$$=C_mH_{m-1}O_3.HO.$$

FROM this formula it is obvious that these acids stand in a close alliance with those which we have described in the commencement of this work;—indeed, we have already associated them with the latter in a single group, to which we have applied the name of fatty acids; but we meet here with the same difficulties which present themselves in inorganic chemistry, in the definition and classification of the metals. Nature recognises no limits corresponding with our artificial systems, but for the purposes of study a separation or arrangement is always useful, provided it be not altogether at variance with nature. These fatty acids have, however, certain essential characters, which distinctly separate them from the first-named acids. Independently of the high atomic weight of the acids we are now considering, and of the circumstance that a very differently constituted group of fluid acids is closely allied to them, the following are the properties which characterise them as a special group. At an ordinary temperature they are solid, white, and crystalline, devoid of smell and taste, leave on paper a fatty spot which does not disappear, are lighter than water, fuse below 100°, can only be distilled unchanged *in vacuo*, are perfectly insoluble in water, dissolve in boiling alcohol, and again separate from it in crystalline forms as the solution cools, dissolve readily in ether, decompose when heated in the air, and are inflammable; their alcoholic solution only faintly reddens litmus; with a gentle heat they expel carbonic acid from its salts; with most bases they form insoluble salts, (the alkaline salts alone being soluble in water,) and they have a strong tendency to form acid salts with bases.

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* Lehrb. d. Ch. Bd. 9, S. 423.

† Pogg. Ann. Bd. 31, S. 399.

‡ Chemie in Anwendg. f. Physiologie.

Very few of these acids have been found in the animal body; one of them, however, *margaric acid*, is the principal constituent of all the fats yet found in the animal body. Associated with it is another fatty acid, *stearic acid*, whose composition, although not in accordance with the above formula, approximates so nearly to it that it may be regarded as produced from 2 equivalents of margaric acid, from which 1 equivalent of oxygen has been abstracted. We place before our readers the whole group of these acids with their chemical formulæ, restricting, however, our observations, to the two above named acids.

Cocinic acid	$C_{22}H_{21}O_3. HO.$
Laurostearic acid	$C_{24}H_{23}O_3. HO.$
Myristic acid	$C_{28}H_{27}O_3. HO.$
Palmitonic acid	$C_{31}H_{30}O_3. HO.$
Palmitic acid	$C_{32}H_{31}O_3. HO.$
Bogic acid	$C_{33}H_{32}O_3. HO.$
Margaric acid	$C_{34}H_{33}O_3. HO.$
Cocostearic acid	$C_{35}H_{34}O_3. HO.$
Behenic acid	$C_{42}H_{41}O_3. HO.$
Cerotic acid	$C_{54}H_{53}O_3. HO.$
Stearic acid	$C_{68}H_{66}O_5.2HO=2C_{34}H_{33}O_3.HO-O$

MARGARIC ACID.—$C_{34}H_{33}O_3.HO$.

Chemical Relations.

Properties.—This acid has all the properties which we have enumerated above as pertaining to this group. It crystallises from a hot alcoholic solution in groups of very delicate nacreous needles, which under the microscope appear interlaced like tufts of grass, and arranged in ensiform plates, or grouped in star-like forms. The acid, when thoroughly dried, fuses at 56°; even when most carefully heated *in vacuo*, it can only be partially distilled unchanged, carbonic acid and *margarone* ($C_{33}H_{33}O$) being always formed; by prolonged contact with nitric acid, it becomes finally decomposed into succinic, suberic and carbonic acids, and water.

Composition.—According to the above formula this acid contains:

Carbon	.... 34 atoms	75·556
Hydrogen	.... 33 „	12·222
Oxygen	.... 3 „	8·889
Water	.... 1 „	3·333
		100·000

The atomic weight of the hypothetical anhydrous acid =3262·5, and its saturating capacity=3·065.

Combinations.—Margaric acid forms both neutral and acid compounds with *alkalies;* the acid salts are principally formed by the addition of much water to the neutral salts; with *oxide of lead* it forms acid, neutral, and basic salts, all of which are soluble in petroleum and oil of turpentine, and the first two in heated alcohol.

Margaramide, $H_2N.C_{34}H_{33}O_2$, is formed when *olive oil* is digested in alcohol saturated with ammonia; it crystallises in fine, silky, glistening needles, is insoluble in water, and is more soluble in hot alcohol and ether than in cold, from which it separates in glistening plates; it fuses at 60°, and when ignited, burns like tallow.

On treating margaric acid with peroxide of lead, Bromeis* obtained a fatty acid which separated in granules and contained 1 atom more of oxygen than margaric acid; its composition being represented by the formula $C_{34}H_{33}O_4.HO$.

Preparation.—Since margaric acid, in the compound which we call margarin, occurs in almost all vegetable fats (the fatty oils) as well as in the most common animal fats, it may be prepared from any of these sources. The best method of obtaining it is to take the fat of man or of the pig, or a vegetable fat, and to saponify it with potash so as to form a clear, viscid, soapy solution; this must be treated with sulphuric acid, which causes a separation of a mixture of stearic, margaric, and oleic acids; this fatty mass must be then well washed with water, dried as thoroughly as possible, and strongly pressed between paper, which causes the removal of a great part of the oleic acid. The solid acids must now be recrystallised in alcohol. The stearic acid is the first to separate from the hot alcoholic solution, and it thus admits of separation and removal; the margaric acid always separates somewhat later; in order, however, that the stearic acid may be perfectly removed, this process must be several times repeated.

We thus obtain margaric acid with no impurity beyond a little oleic acid, which may be removed by saturating the acids with an alkali and precipitating with acetate of lead; as the oleate of lead is soluble in boiling ether, while the margarate of lead is insoluble, we have an easy means of separating the two salts. The margarate of lead must then be decomposed by an alkaline carbonate, and the resulting alkaline salt by a stronger acid. The margaric acid which is thus separated may be further purified by solution in hot alcohol.

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* Ann. d. Ch. u. Pharm. Bd. 42, S. 56.

Tests.—From the properties, as well as from the mode of preparing this acid, we perceive that it can only be distinguished from other similar acids when it is perfectly free from any admixture with them: we may derive some information on this head from its boiling point; but it is only by an elementary analysis that we can arrive at any certain conclusion. In the investigation of small quantities, when a separation or an analysis is out of the question, we must trust solely in a microscopical examination, which, however, in this case yields by no means such uncertain results as is generally supposed.

Physiological Relations.

Occurrence.—It has already been remarked that margaric acid is the principal constituent of most animal fats; but this acid is here ordinarily combined with the hypothetical haloid base, *oxide of lipyl*, which, in its separation from this and similar acids, is converted into the well-known body, glycerine. Of margarin itself we shall speak in a future part of this volume, and we shall consequently defer for the present all remarks on the physiological function of margaric acid and its organic salts. But margaric acid occurs both in a free state and in combination with alkalies in most of the animal fluids, with the exception of urine; being free in acid fluids, and in a state of combination in those with an alkaline reaction; it is always accompanied by oleic acid or its salts. Its presence in the saliva, in the blood, in exudations of all kinds, in pus, and in the bile, is so easily recognised, that it is unnecessary to quote authorities regarding its existence in these fluids; moreover, in our remarks on these fluids we shall return to this subject. We will here only remark that it may also be discovered in the solid excrements after the use of vegetable food, and that it occurs in considerable quantity in dejections which have been caused by purgatives or mineral waters. As already mentioned, we must here always have recourse to the microscope, by which, independently of any chemical process, free margaric acid may often be detected in acid pathological fluids; thus, in acid pus discharged from what are termed cold abscesses, or in pus in which acid fermentation has with all due caution been established, the most beautiful crystals of margaric acid are formed; more beautiful indeed than we could artificially prepare.

We shall postpone our observations regarding the *origin* of margaric acid in the animal organism, and the *rank* and *position* it holds in the metamorphosis of the animal tissues, till we take into consideration the formation and the physiological importance of the fats in the animal body.

STEARIC ACID.—$C_{68}H_{66}O_5.2HO$.

Chemical Relations.

Properties.—This acid crystallises in white, glistening needles or leaflets, which, however, under the microscope, appear as very elongated, lozenge-shaped plates, with the obtuse angles rounded off, as in the microscopical whet-stone-like crystals of uric acid; these crystals are, however, much longer, and have a far shorter transverse diameter than the similar crystals of uric acid. They often collect at one spot, the acute angles slightly overlapping one another, so that when seen under the microscope the crystals present the arrangement of whorl-shaped clusters. This acid begins to fuse at 75°, but again solidifies if the temperature is reduced to 70°. Submitted to dry distillation it yields hydrated margaric acid, margarone, and an oleaginous carbo-hydrogen; by prolonged digestion with nitric or chromic acid it becomes perfectly converted into margaric acid. In the cold, stearic acid decomposes the carbonated alkalies to the amount of one-half, but with the aid of heat a perfect decomposition is effected.

Composition.—According to the above formula, stearic acid contains:

Carbon	.... 68 atoms	76·692
Hydrogen	.... 66 „	12·406
Oxygen	.... 5 „	7·519
Water	.... 2 „	3·383
		100·000

The atomic weight of the hypothetical dry acid = 6425 : its saturating capacity, (if we regard as neutral the salt containing 2 atoms of base) = 3·113.

Combinations.—The neutral alkaline stearates (containing 2 atoms of fixed base) dissolve unchanged in from 10 to 20 parts of water; in a very large quantity of water they become decomposed, an acid salt separating, and the fluid becoming very strongly alkaline; the alcoholic solution of the acid salt reddens litmus, but on the addition of water to this solution the reddened litmus again becomes blue. The compounds of stearic acid with all other bases are insoluble in water. For *stearate of oxide of lipyl* (or *of glycerin*) see "Stearin."

Preparation.—As this acid does not occur in vegetable fats, and exists only in very small quantity in most of the animal fats, except in mutton fat, it is from this last-named source that it is most advantageously prepared; we obtain it in accordance with the method indicated in our remarks on margaric acid, by boiling with alcohol of 0·83 spec. grav. the fatty acids separated by sulphuric acid from the soap; this leaves a residue of stearic acid tolerably free from margaric acid; by repeated solution in absolute alcohol it becomes purified, till we finally obtain a mass possessing the known fusing point of this acid. The following method of preparing it may also be recommended. Dissolve saponified mutton fat in 6 parts of warm water, and then wash it well with a large quantity of cold water; a gradual separation of a glistening nacrous mass now ensues, consisting of bistearate and bimargarate of potash. This must be dissolved in 20 times its bulk of hot alcohol, from which, as it cools, the stearate alone separates; on decomposing this salt with hydrochloric acid, the free acid may be obtained by remelting it in water.

Tests.—An elementary analysis can only be instituted as a test for the presence of stearic acid, when there is a sufficiently large quantity of fat present to admit of the above-mentioned separation of stearic and margaric acids,—a separation which, unfortunately, is only practicable when we have very large quantities to deal with. Hence this, the most certain method, is only applicable in determining the amount of stearin in an animal fat. In dealing with smaller quantities we must rest content with the microscopic investigation of the fatty acids separated from hot alcoholic solutions. In order to obtain a scale for the approximate ratios of a mixture of margaric and stearic acids, Gottlieb* has determined the fusing points of various mixtures of these acids. His results are as follows:

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* Ann. d. Ch. u. Pharm. Bd. 57, S. 35.

		Stearic acid		Margaric acid		Fusing point
1)	....	30 parts	to	10 parts	....	65°·5
2)	....	25 „	„	10 „	....	65°
3)	....	20 „	„	10 „	....	64°
4)	....	15 „	„	10 „	....	61°
5)	....	10 „	„	10 „	....	58°
6)	....	10 „	„	15 „	...	57°
7)	....	10 „	„	20 „	....	56°·5
8)	....	10 „	„	25 „	....	56°·3
9)	....	10 „	„	30 „	....	56°

Both pure margaric and pure stearic acids, after having been fused and again allowed to solidify, are perfectly crystalline; stearic acid, however, forms small confused crystals, while margaric acid forms larger acicular crystals; a mixture of the two acids is however, in this state, far less crystalline, and presents rather a porcelain-like, opaque, and brittle appearance.

Physiological Relations.

Occurrence.—Like margaric acid, stearic acid occurs in most animal fats; it is, however, always found in less quantity than margaric acid, and in some cases appears to be altogether absent; or, at least, our present chemical appliances fail in detecting it. In the fat of the cellular tissue it exists like margaric acid in combination with glycerine; it never occurs free unless in association with margaric acid; it is, however, of much rarer occurrence than free margaric acid, and occurs in much smaller quantity.

Origin.—As stearic acid is never found in vegetable fats, it must be primarily formed in the animal body, where, indeed, its formation may be readily explained. As it consists of 2 atoms of margaric acid *minus* 1 atom of oxygen, we may regard it as produced from margaric acid, to which it stands, as we have seen, in the same relation as hyposulphuric acid to sulphuric acid, for $S_2O_5 : SO_3 = (C_{34}H_{33})_2O_5 : (C_{34}H_{33})O_3$.

In which part of the system this conversion occurs we do not at present know: that it takes place in the blood is improbable, because we assume that the fats are directly oxidised in the blood, and are decomposed into the oxides of simpler radicals. That this conversion takes place in the *primæ viæ* is, at all events, incapable of demonstration.

We shall speak of the uses of stearic acid in the animal organism, in our remarks on the fats in general.

OILY FATTY ACIDS.

$=C_mH_{m-3}O_3.HO.$

This group of bodies contains a far smaller number of members than the preceding groups. At present the following are the only oily fatty acids with which we are acquainted :

Oleic acid	$C_{36}H_{33}O_3.HO.$
Erusic acid	$C_{44}H_{41}O_3.HO.$
Doeglic acid	$C_{38}H_{35}O_3.HO.$

Ricinoleic acid, containing the same group of atoms of carbon and hydrogen with 5 atoms of oxygen ($=C_{38}H_{35}O_5.HO$), bears the same ratio to the last of these acids, which salicylous acid bears to benzoic acid.

Dissimilar as, on the whole, is the composition of the oily and the solid fatty acids, they are yet similar in most of their physical and even in many of their chemical properties.

Whether *campholic acid* $C_{20}H_{17}O_3.HO$, and the two isomeric acids, *campheric acid* and *angelic acid*$=C_{10}H_7O_3.HO$, belong to this group (for their composition accords with the general formula $C_mH_{m-3}O_3.HO$) is as yet undecided; several of their physical properties (for instance, they are solid, crystallisable, and volatile,) do not accord with this view, but these acids may possibly bear the same relation to the oily acids, that the acids of the first group bear to the solid fatty acids, and the low atomic weight of the radical may also be the cause of this difference in their properties.

OLEIC ACID.—$C_{36}H_{33}O_3.HO.$

Chemical Relations.

Properties.—This body, known also as elaic acid, is, when perfectly pure, and at a temperature above + 14°, of an oily consistence, limpid, devoid of colour, taste, and smell, and exerts no action on litmus ; at + 4° it forms a white, crystalline mass, which, at the moment when it solidifies, strongly contracts and expresses the still oily portion ; it is then very hard, and is unaffected by exposure to the atmosphere ; on exposing an alcoholic solution to extreme cold it crystallises in long needles. In its fluid condition, that is to say, as oil, it rapidly absorbs oxygen and becomes changed. When heated, it becomes decomposed, yielding not only carbon,

carbon, carbonic acid, and carbo-hydrogens, but capric and caprylic acids, and especially sebacic acid. Finally, on treating oleic acid with hyponitric acid, the whole mass becomes solid and converted into elaidic acid. By prolonged treatment with nitric acid, oleic acid yields (according to Laurent* and Bromeis†) the acids of the succinic acid group ($C_nH_{n-2}O_3.HO$) namely, suberic, adipic, pimelic, and lipic acid, and, besides these, œnanthylic acid, but no oxalic acid. With fuming nitric acid it yields, on the other hand, according to Redtenbacher‡ almost all the acids of the first group ($C_nH_{n-1}O_3.HO$).

In the oily products of the dry distillation of oleic acid Schneider§ found that the atoms of carbon were to those of hydrogen in the ratio of 6 : 5 ; and on treating these products with concentrated nitric acid, he obtained the same volatile acids which Redtenbacher obtained by the direct action of nitric acid on oleic cid.

Composition.—According to the above formula this acid conains:

Carbon	36 atoms	76·596
Hydrogen	33 „	11·702
Oxygen	3 „	8·511
Water	1 „	3·191
		100·000

The atomic weight of the hypothetical anhydrous acid = 3412·5 ; its saturating capacity = 2·930.

Combinations.—The *oleates* are soft and greasy, and do not crystallise; like all the fatty acids, oleic acid has a strong tendency to form acid as well as basic salts. The neutral *oleate of lead* is a white powder which fuses at 80° into a yellow fluid, and is distinguished, by its solubility in boiling ether, from the lead-salts of all the solid fatty acids.

Products of its Metamorphosis.—Gottlieb,‖ who was the first to obtain pure oleic acid, and who, from his analyses, deduced the above formula, states that at an ordinary temperature, and when freely exposed to the atmosphere, this acid absorbs about 20 times its volume of oxygen, *without developing carbonic acid.* The thick fluid acid which is thus formed, and which now reddens litmus, contains 1 atom more of oxygen and 1 atom less of hydrogen than the pure oleic acid, being represented by the formula $C_{36}H_{32}O_4.HO$. This acid yields no *sebacic acid* on dry distillation. Hence it is that oleic acid, when not perfectly pure, that is to say, when changed by the access of oxygen, often yields only very little *sebacic acid*, while the quantities of capric and caprylic acids which are developed, remain constant.

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* Ann. d. Chim. et de Phys. T. 66, pp. 154-204.

† Ann. d. Ch. u. Pharm. Bd. 35, S. 86-103.

‡ Ibid. Bd. 59, S. 41-57.

§ Ibid. Bd. 70, S. 107-121.

‖ Ibid. Bd. 57, S. 37-67.

If, however, oleic acid be exposed at a higher temperature to the action of oxygen, it rapidly assumes a rancid odour, becomes yellowish and more easily fusible, does not solidify so perfectly when exposed to cold, and its composition is represented by the formula $C_{34}H_{33}O_5$; hence it may be regarded as a higher stage of oxidation of the radical of margaric acid than that obtained by Bromeis, and noticed in page 107.

Elaidic acid is, according to Gottlieb, perfectly isomeric with pure oleic acid, and is therefore represented by the formula $C_{36}H_{33}O_3.HO$. It is produced, as we have already mentioned, from oleic acid by the action of nitrous acid, without any development of gas; it crystallises from an alcoholic solution, not in needles like oleic acid, but in large plates; it fuses at 45°, may be partially distilled undecomposed, dissolves readily in ether and alcohol, and strongly reddens litmus. On dry distillation elaidic acid yields no caprylic and capric acids, in which respect it differs essentially from oleic acid. In the fluid state this acid abstracts oxygen from the air, although less rapidly than oleic acid, and becomes converted, according to Gottlieb, into a higher stage of oxidation of the same radical, which we may assume to exist in oleic and elaidic acids, namely into $(C_{36}H_{33})O_8$. How the metamorphosis of oleic into elaidic acid exactly takes place, or on what it depends, are points on which as yet we have no certain knowledge.

Preparation.—This acid also is obtained by the saponification of vegetable and animal fats; the oleate of potash is extracted from the soap with cold absolute alcohol; the aqueous solution of oleate of potash is then precipitated with acetate of lead, and the oleate of lead (free from the margarate) is taken up from the dried precipitate by boiling ether. If the lead-salt, after the removal of the ether, be decomposed with carbonate of soda, and if the resulting soda-salt be decomposed with sulphuric acid, we obtain a somewhat brownish oleic acid mixed with products of oxidation. In order to obtain the acid in a state of perfect purity, we must, according to the directions of Gottlieb, treat it with an excess of ammonia, and precipitate it with chloride of barium: the baryta-salt is then to be repeatedly crystallised in moderately concentrated boiling alcohol, till it form a dazzling white flocculent powder, which must be decomposed with tartaric acid and thoroughly washed with water. Pure oleic acid may be more rapidly obtained by causing it to solidify by exposing it to a temperature of 6° or 7°, and then submitting it to strong pressure; as the above-mentioned products of oxidation of oleic acid remain fluid, they become absorbed in the filtering paper, and leave the oleic acid in a state of purity. Further, the water must only be removed while the oleic acid is exposed to a stream of carbonic acid, and all operations upon it should be conducted at a temperature below $+10^\circ$, since it very rapidly becomes decomposed.

Tests.—If it be required to test a fat or a mixture of fatty acids accurately for oleic acid, we must first isolate this acid by one of the methods which we have described, and obtain it in a state of at least tolerable purity, so as to enable us to ascertain the solubility of the lead-salt in hot ether. Moreover, oleic acid possesses the distinctive character of being the only one either of the oily or solid fatty acids which, on dry distillation, yields *sebacic acid*—an acid which may be distinguished from the simultaneously formed capric and caprylic acids by its crystallisability, and which we may easily separate from them and recognise, by forming and crystallising its baryta-salt.

Physiological Relations.

Occurrence.—Oleic acid, in combination with alkalies, exists in the blood and in the bile, and, in lesser quantity, in most of the other animal fluids, except the urine: in combination with oxide of lipyl, as a haloid salt, it occurs in the fat of the cellular tissue, and, indeed, wherever free fat is found in the animal body.

Uses.—As the vegetable fats are, for the most part, far richer in oleate of oxide of lipyl (olein) than animal fats, there seems to be a reason for the assumption that one of the uses of oleic acid in the animal body, is to form the more solid fats, margaric and stearic acids;—a view which is supported by the nature of the action of atmospheric air on oleic acid, (to which we have already referred,) and by its conversion into an acid having the radical of margaric acid. It might, however, have been expected *à priori* that animal fat would contain more margarate than oleate of oxide of lipyl, since oleic acid or an oleate is more rapidly consumed than margaric acid. We must, however, here, as in many other departments of physiological chemistry, rather abstain wholly from all conjectures than allow ourselves to be led astray by mere fancy. Let us rather wait for further facts to serve as substrata on which to establish a strictly logical hypothesis. Generally speaking, the function of oleic acid in the animal body coincides with that of the other fatty acids: but we shall return to this subject in a future part of this volume.

Origin.—In our remarks on the fats, we shall consider the question whether the animal body possesses the power of forming margaric and oleic acids as well as stearic acid.

DOEGLIC ACID.—$C_{38}H_{35}O_3 . HO$.

This acid, which was discovered by Scharling [*] in the train oil of *Balæna rostrata,* is obtained from the lead-salt which is taken up by ether, precisely in accordance with Gottlieb's method of purifying oleic acid. At + 16° it is perfectly fluid, but solidifies at a few degrees above 0°: it is yellow and reddens litmus; on dry distillation it yields *no sebacic acid.* This acid is, moreover, not combined with oxide of lipyl in the Doegling train-oil, (at least it yields no glycerine on saponification,) but probably with *doeglic oxide,* $C_{24}H_{25}O$, a body similar to the ether-like haloid bases, whose existence and composition Scharling, however, only infers from the analysis of the unsaponified Doegling train-oil and the absence of glycerine.

NON-NITROGENOUS RESINOUS ACIDS.

LITHOFELLIC ACID.—$C_{40}H_{36}O_7 . HO$.

Chemical Relations.

Properties.—This acid crystallises in small, six-sided, right prisms, is readily pulverisable, fuses at 205°, and solidifies again in a crystalline form, if it has not been too highly heated; if, however, this has been the case, it solidifies into a vitreous, negatively idio-electric mass; in this condition it fuses at 105° to 116°; by solution in, or mere moistening with, alcohol, it returns to its former condition, being difficult to fuse again; when heated in the air, it volatilises in white vapours with an aromatic odour; when inflamed it burns with a bright, smoky flame; it is decomposed by dry distillation; it is insoluble in water, dissolves readily in hot alcohol, but only slightly in ether; acetic acid dissolves it freely; acids precipitate it from its soluble salts as an amorphous coagulum.

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[*] Journ. f. pr. Ch. Bd. 43, S. 257-271.

Composition.—Ettling and Will,* from their analyses, calculated for it the formula $C_{42}H_{36}O_8$; Wöhler,† from his analyses, deduced the formula $C_{40}H_{36}O_8$; and Berzelius,‡ judging from the saturating capacity of the acid, considers the formula $C_{40}H_{36}O_7.HO$ as the most correct: hence it must be regarded as containing:

Carbon	.... 40 atoms	70·381
Hydrogen	.... 36 "	10·557
Oxygen	.... 7 "	16·422
Water	.... 1 "	2·640
		100·000

Hence the atomic weight of the hypothetical anhydrous acid (according to the above formula) =4150, and its saturating capacity =2·41.

Combinations.—This acid dissolves readily both in caustic ammonia and in carbonate of ammonia, but on evaporation of the solution it remains free from ammonia; the salts of baryta and lime throw down no precipitate from this solution: moreover, it dissolves readily in caustic potash, but is precipitated by an excess of potash as well as by hydrochlorate of ammonia; on the addition of the salts of lead or silver to a saturated potash-solution of this salt with only a faintly alkaline reaction, there is a white precipitate which, on warming, becomes plaster-like. Ettling and Will have obtained a silver-salt which crystallised in needles; Wöhler, however, only obtained an amorphous salt.

Preparation.—This acid, which was originally discovered by Göbel,§ is extracted from certain intestinal concretions by hot

* Ann. d. Ch. u. Pharm. Bd. 39, S. 237-244.

† Pogg. Ann. Bd. 54, S. 255.

‡ Jahresber. Bd. 22, S. 580.

§ Ann. d. Ch. u. Pharm. Bd. 39, S. 237.

alcohol; the solution is decolorised by animal charcoal, and gradually evaporated.

Tests.—This acid may be recognised with tolerable certainty by the properties which we have already enumerated. If, however, it be found in other places than in intestinal concretions, it should always be submitted to an elementary analysis.

Physiological Relations.

Occurrence.—According to the researches of Merklein and Wöhler,* as well as those of Taylor,† this body exists only in certain bezoars, which are obtained from the intestines, and especially from the stomach of many species of goats inhabiting the East; other bezoars contain ellagic acid.

Origin.—Whether lithofellic acid takes its origin in the bile, or is dependent on the use of resinous food, is as yet undecided, since its similarity to the resins is as great as to the resinous acids of the bile. Its analogy with ellagic acid certainly speaks in favour of its origin from the food; if, however, Taylor's view, that concretions containing lithofellic acid are frequently found in the stomach, be confirmed, it is obvious that they cannot owe their origin to the bile.

CHOLIC ACID.—$C_{48}H_{39}O_9.HO$.

Chemical Relations.

Properties.—This acid crystallises in tetrahedra, and more rarely in square octohedra, is colourless, glistening, and easily pulverised; the crystals effloresce on exposure to the air; the acid is bitter, leaving a faint sweetish after-taste; it is soluble in 750 parts of boiling, and in 4000 parts of cold water; it dissolves very readily in alcohol, especially when heated, and in 27 parts of ether. The acid, in crystallising from ether, forms rhombic tablets, and in this form it contains 2 atoms of water, while from alcohol it crystallises in tetrahedra with 5 atoms of water; the acid separated from alcohol by the addition of water contains 2 atoms of water, which it loses at 100°, while the tablets only lose 1 atom at that temperature. Moreover, this acid strongly reddens litmus, fuses at 195°, and at a higher temperature undergoes decomposition; above 195° it loses its atom of basic water, and is converted into choloidic acid, and at 290° it becomes converted into dyslysin (Strecker*); when inflamed it burns with a clear flame. It dissolves in sulphuric acid; and if to this solution we add a drop of syrup (1 part of sugar to 4 of water), the fluid assumes a beautiful purple-violet tint. If cholic acid be boiled for some time with hydrochloric acid it ceases to be crystallisable, and is converted into the resinous *choloidic acid;* and on further prolonging the boiling, the body, at the same time that it loses its solubility in alcohol and alkalies, also parts with its acid properties and then forms *dyslysin.* By the action of boiling nitric acid, it is for the most part converted into capric, caprylic, and cholesteric acids, without yielding oxalic acid or the volatile acids of the first group.

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* Ann. d. Ch. u. Pharm. Bd. 55, S. 129-143.

† Lond., Edinb., and Dubl. Phil. Mag. vol. 28, pp. 192-200.

Composition.—This acid, which was first obtained in a state of purity by Demarçay, has been recently examined with much care by Strecker.† He found that it was constituted in accordance with the above formula. It consequently consists of:

Carbon	48 atoms	70·588
Hydrogen	39 „	9·559
Oxygen	9 „	17·647
Water	1 „	2·206
		100·000

Consequently the atomic weight of the hypothetical anhydrous acids =4987·5, and its saturating capacity=2·005.

Mulder,‡ from his analyses of this acid, has deduced for it the the formula, $C_{50}H_{36}O_6+5HO$.

Strecker, who by his admirable memoir on the bile of the ox, has done so much to advance our knowledge regarding this very obscure fluid, has unfortunately increased the existing confusion regarding cholic acid by giving it the new name of *cholalic acid,* while he applies the name of cholic acid to another acid which we shall subsequently describe. It is, however, true that Gmelin applied the term cholic acid to that acid of the bile in whose salts he recognized a sweet taste, and regarded it as a nitrogenous acid; but the non-nitrogenous acid first obtained in a state of purity by Demarçay, which in its mode of preparation and in its properties is identical with that which is here described, has so long been known as cholic acid that this name ought to be retained, and the more so because the new name of cholalic acid is by no means more expressive of its nature. We therefore retain the denomination which Demarçay, its discoverer, applied to it.

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* Ann. d. Ch. u. Pharm. Bd. 58, S. 375-378.

† Ibid. Bd. 66, S. 1-61.

‡ Unters. üb. d. Galle, übers. v. Völkel., Frank. a. M. 1847. S. 26.

Combinations.—The *cholates* possess a bitter and at the same time a slightly sweet taste; they are all soluble in alcohol, but water dissolves only the alkaline cholates and cholate of baryta, and, to a very slight extent, cholate of lime. Cholic acid, with the aid of heat, expels the carbonic acid from solutions of the alkaline carbonates.

Cholate of potash, $KO.C_{48}H_{39}O_9$ is obtained in acicular crystals, by the evaporation of the alcoholic solution, or by the addition of ether to it. By spontaneous evaporation of the aqueous solution it forms a kind of varnish; the salt is insoluble in an excess of solution of potash, and on the addition of caustic potash is precipitated in a gelatinous state. *Cholate of soda* and *cholate of ammonia* are very similar to it; the latter of these two salts loses the greater part of its ammonia on mere evaporation. *Cholate of lime*, when obtained by precipitation, is amorphous, but it crystallises on the addition of ether. *Cholate of silver* is only very slightly soluble in water; it crystallises, however, from a boiling solution.

Products of its metamorphosis.—*Choloidic acid*, as it exists in its salts, is perfectly isomeric with cholic acid; it is formed as we have already mentioned, by boiling cholic acid with stronger acids. It may, however, be obtained by boiling together for some hours hydrochloric acid and that portion of the alcoholic extract of bile which is precipitable by ether; by solution in alcohol and precipitation by ether, it may be readily purified. It is a peculiarity of choloidic acid that in its isolated state it contains no basic water, and may therefore be prepared in an actually anhydrous state; it forms a white, amorphous, resinous, pulverisable mass which is insoluble in water, but dissolves freely in alcohol, and slightly in ether. The addition of water or of ether to the alcoholic solution causes a milky appearance, and finally precipitates the acid in a resinous form; the alcoholic solution reddens litmus. When warmed, choloidic acid softens; at 150° it fuses, and at 295° it becomes converted into dyslysin, with the loss of 3 atoms of water. With concentrated sulphuric acid and sugar it gives the same reaction as cholic acid. When distilled with nitric acid, it yields not only the same volatile acids as oleic acid when similarly treated, but additionally choloidanic, cholesteric, and nitrocholic acids, and cholacrole (Redtenbacher.*)

Its *salts* have a purely bitter taste, without any sweet after-taste; the acid is displaced from them by stronger acids, and even by carbonic acid, although, on the other hand, choloidic acid expels carbonic acid when heated with carbonates. The alkaline salts of this acid are soluble in water and in alcohol, but not in ether; they cannot be obtained in a crystalline state. *Choloidate of baryta*, although isomeric with the cholate, is not crystallisable, and is insoluble in water. With earths and metallic oxides this acid forms salts which are soluble in alcohol but insoluble in water.

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* Ann. d. Ch. u. Pharm. Bd. 57, S. 145-170.

Dyslysin $C_{48}H_{36}O_6$ (Strecker), $C_{50}H_{36}O_6$ (Mulder,) is obtained from cholic or choloidic acid by one of the methods which we have already mentioned; the mass thus formed is extracted with water and alcohol, and dissolved in ether, from which it is again precipitated by alcohol; it is now of a grayish-white colour, and the extent of its solubility depends upon the degree of its purity; it is, however, insoluble in acids and alkalies. When fused with hydrate of potash, or boiled with an alcoholic solution of potash, dyslysin is reconverted into choloidic acid.

From the choloidic acid of Demarçay, Berzelius has separated two acids, which he has named *fellic* and *cholinic acids*;* he, like Mulder, regards choloidic acid as an admixture of these two acids; it is to be regretted that Strecker, in his otherwise admirable investigation, has not made that reference to these substances which they deserve; for other chemists as well as Mulder may repeat the experiments and confirm the statements of Berzelius. We shall content ourselves in the present place, with indicating the most important points of difference between these two acids.

Cholinic acid ($C_{50}H_{38}O_8$ Mulder) forms white and bright flocculi, insoluble in water, and which, on drying, become brown and pulverisable. Its baryta and lead-salts have a tendency to cake together, and are *almost insoluble in alcohol;* the ammonia-salt of this acid separates as a white, saponaceous mass.

Fellic acid ($C_{50}H_{40}O_{10}$) forms snow-white flocculi, which when dried become pulverisable; it is slightly soluble in water, and its solubility in ether is even less than that of cholinic acid. Its baryta and lead-salts are *soluble in alcohol.*

Redtenbacher distilled nitric acid over choloidic acid as long as vapours of nitrous acid continued to be developed, and he found in the receiver acetic, butyric, valerianic (?) caproic, œnanthylic, caprylic, pelargonic, and capric acids (precisely the same as he obtained when oleic acid was similarly treated), and besides these, a heavy, stupifying oil, which, when treated with alkalies, was decomposed into *nitrocholic acid* and *cholachrole;* while in the retort there remained, as if proof against the further action of nitric acid, *oxalic, choloidanic* and *cholesteric* acids.

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* [In the German these acids are termed *Fellinsäure* and *Cholinsäure:* we adopt the phrase *cholinic acid* for the latter word, as *cholic acid* is a pre-engaged name.—G. E. D.]

Cholacrole, $C_8H_5N_2O_{13}$, is a yellow oil with a pungent, overpowering, cinnamon-like odour, dissolving readily in alcohol and ether, but difficult of solution in water; it is indifferent towards both acids and alkalies, and is decomposed at 100° with the development of nitrous acid, and sometimes with slight decrepitation.

Nitrocholate of potash, $KO.C_2HN_4O_9$, occurs in lemon-yellow, square tablets, has a faintly overpowering odour, decrepitates at 100°, is decomposed when boiled with water, and is not precipitated by metallic salts.

On pouring into a large test glass the thick, brownish yellow mass which remains in the retort, it separates on cooling into two layers, of which the upper is frothy, and consists of crystals of choloidanic acid, while the lower is of a yellowish brown colour, acid and bitter.

Choloidanic acid, $C_{16}H_{12}O_7$, crystallises in satiny, hair-like prisms; when dry, it resembles asbestos; it is difficult of solution even in hot water, but dissolves freely in alcohol; it reddens litmus, and is decomposed at a high temperature, but is unaffected by hydrochloric or nitric acid. Its salts, even those of the alkalies, are insoluble or difficult of solution, and do not crystallise.

In this yellowish brown mother-liquid there are also contained oxalic acid, a resinous mass, and cholesteric acid.

Cholesteric acid, $C_8H_4O_4.HO$, occurs as a light yellow mass, resembling cherry-gum; it has a well-marked acid and bitter taste, abstracts water from the air, dissolves both in water and in alcohol, the solution being of a yellow tint, and decomposes when heated; its compounds with alkalies and alkaline earths do not crystallise, and are soluble in water, but its compounds with metallic oxides are insoluble. The silver-salt dissolves in boiling water, from which it is deposited, on cooling, in crystalline incrustations.

Preparation.—Cholic acid, which occurs in the bile conjugated with nitrogenous bodies, is most readily obtained by boiling the resinous masses precipitated by ether from the alcoholic solution of the bile with a dilute solution of potash for twenty-four to thirty-six hours, till the potash-salt that has separated begins to crystallise. The potash-salt must then be dissolved in water and the acid removed from it by hydrochloric acid. By the addition of a few drops of ether, the acid which was previously resinous becomes crystalline, solid, and admits of trituration; it must be pulverised, washed with water, recrystallised in alcohol, and finally treated with a little ether in order to remove any colouring matter that may be attached to it.

Tests.—Cholic acid even when not perfectly pure may be recognised by its reaction with sugar and sulphuric acid. This reaction, which was first discovered by Pettenkofer,* occurs with no other substance than cholic acid; it is, however, perfectly immaterial whether the cholic acid be already metamorphosed into choloidic acid, or whether it be combined with its adjuncts, as a conjugated acid. Hence we can apply this admirable test to discover generally either the presence of bile or of one of its derivatives. The following is the best method of proceeding. The alcoholic extract of the fluid to be tested for biliary matter must be dissolved in a little water, with which we must then mix a drop of a solution of sugar, (in the proportion of 1 part of sugar to 4 of water); and pure English sulphuric acid, free from sulphurous acid, must be added by drops to the mixture; the fluid now becomes turbid from the separation of the cholic acid, but on the gradual addition of sulphuric acid the turbidity disappears, and the fluid again becomes perfectly clear; for the first few moments its colour is yellowish, it very soon however becomes of a pale cherry colour, then of a deep carmine, of a purple, and finally, of an intense violet tint. As, indeed, in all experiments, some practice and attention to certain rules are requisite, without which we may easily fail to apply this test successfully to the detection of bile. For instance, we must avoid the addition of too much sugar, as this is a substance which is easily rendered brown or black by sulphuric acid; and we must be especially careful, as Pettenkofer himself showed, while adding the concentrated sulphuric acid, not to allow the temperature much to exceed 50°; but the reaction equally fails when we carry our caution too far, and attempt to avoid any elevation of temperature when the sulphuric acid is added; indeed, my own experience leads me to believe that an elevation of the temperature nearly to 50° is requisite for the success of the experiment. Should the fluid at first assume only a cherry-red or a deep carmine tint, it must be allowed to stand for some time, after which the intense violet colour becomes developed. It is, moreover, immaterial which kind of sugar is used for this test: acetic acid may also be employed in place of sugar.

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* Ann. d. Ch. u. Pharm. Bd. 53, S. 90-96.

Van den Broek* maintains that the reaction also takes with mere biliary matter independently of the sugar, but I have never found this to be the case; without sugar the fluid has at most attained a red or reddish brown tint, but never the characteristic, deep violet colour. But although van den Broek is wrong on this point, there are other reasons why his view is correct, that this reaction is inapplicable as a test for sugar; in the first place, because we have the same reaction when other bodies, as for instance, acetic acid, are substituted for sugar, and, secondly, because we have many better and more certain means of discovering this substance.

If it should be necessary to separate the cholic acid from the conjugated biliary acids, or from choloidic acid, as is sometimes required in the examination of the blood, urine, and excrements, the best method is to acidulate the alcoholic extract with a little sulphuric acid, and to extract with ether, in which the conjugated biliary acids and choloidic acid are all but insoluble. As the cholate of baryta is soluble and crystallisable, which is not the case with the choloidate, we may thus as well as by the crystallisability of free cholic acid, readily distinguish between cholic and choloidic acids; the biliary acids are not only perfectly insoluble in ether, but one of them, when boiled with potash, yields ammonia, and the other, when similarly treated with hydrochloric acid, yields taurine, which, as we shall presently show, may be easily recognised under the microscope by the form of its crystals.

Physiological Relations.

Occurrence.—In the *bile* we neither find cholic nor choloidic acid isolated from its respective adjunct; hence either within the animal body, in the gall-bladder, or after removal from the organism, it seems to have already passed into a state of decomposition, or else one of these acids must have been produced by the chemical treatment to which the bile has been subjected.

In examining the *blood* and the *urine* of patients suffering from diseases in which the liver is not directly implicated, we not unfrequently meet with substances yielding the above-described reaction for bile; I have, however, never satisfied myself in such cases, by any method, that either the one or the other of the biliary acids could be recognised with certainty. We shall treat more fully of the occurrence of these biliary matters in the blood and urine in our observations on the conjugated biliary acids. (See also "Blood" and "Urine.")

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* Holländische Beiträge. Utrecht u. Düsseld. 1846. S. 100-102.

In healthy *solid excrements* Pettenkofer* found no substance yielding this biliary reaction; the dejections in cases of diarrhœa, on the other hand, always contained a substance yielding this reaction. I have, however, always been able to detect a little cholic acid in perfectly normal excrements.

The alcoholic extract of previously dried solid excrement presented no reaction with sulphuric acid and sugar; but on further treating this extract with ether, and on purifying the residue of the ethereal solution, by means of water, from the fatty acids which are always mixed with it, I found that the somewhat concentrated aqueous solution (of this ethereal extract) presented the biliary reaction most beautifully. On using a larger quantity of material, the acid was obtained in a crystalline state; as it yielded no ammonia when treated with potash, and as its baryta-salt was soluble, it could hardly have been any other than cholic acid.

In the *intestinal canal* we can detect the presence of bile in the contents of the whole of the small intestine, by the addition of sulphuric acid to the alcoholic extract, in the manner above described.

If I rightly recollect, Pettenkofer informed me, in a private communication, that he had already made this observation. I have repeatedly convinced myself of its accuracy in animals; in the case of an intestinal fistula, where it could not be determined with certainty whether the perforation was in the small or large intestine, and where no conclusion could be drawn from the absence of villi, the diagnosis was established by the bile-test. It was subsequently proved that the fistula occurred in the small intestine.

That substances containing or yielding cholic acid sometimes occur in *exudations*, requires no proof, as the blood is frequently overloaded with such matters.

I will here only mention that in the dropsical exudations occurring in a case of granular liver, and in another case of insufficiency of the mitral valves with stoppage of the biliary ducts, I found a considerable quantity of biliary matter. This subject is more fully noticed in the chapter on "Exudations."

The presence of biliary matters in morbid *saliva* and *expectoration*, is asserted by Wright,† but has not been proved.

Origin.—As we must return, in a future page, to the different opinions which are maintained regarding the origin of the essential constituents of the bile, we shall here only notice such points as chemically elucidate the formation of cholic acid. That cholic and choloidic acids proceed from conjugated biliary acids, has been already mentioned; but according to the theoretical views which are at present maintained, cholic acid exists preformed in these biliary acids, just as in every conjugated acid we regard the true acidifying group of atoms as already formed. Without alluding here to the question whether the bile is primarily formed in the blood or in the cells of the liver, we will merely enquire what substances in the animal body yield that group of atoms which we call cholic acid? Even if many physiological and pathological facts did not support the view that the fats yield the principal material for the formation of the bile, the experiments of which we have made mention regarding the products of oxidation of cholic and choloidic acids, would lead us to the belief that these bodies are closely allied to the fats, and especially to oleic acid; for we have seen that Redtenbacher has obtained from choloidic acid when treated with nitric acid precisely the same volatile acids (of the first group) as were yielded by oleic acid under similar treatment, independently of other specific substances. These latter may appropriately be regarded as arising from a group of atoms still hidden in the cholic acid, which group must be assumed to be an adjunct in the cholic acid. For if it be not improbable that such simple acids as acetic acid, butyric acid, &c., are to be regarded as conjugated acids, we are almost compelled to regard an acid like cholic acid with so high an atomic weight, and so considerable an amount of oxygen (that is to say, with so small a saturating capacity) as a conjugated acid.

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* Ann. d. Ch. u. Pharm. Bd. 53, S. 90-96.

† The Lancet, 1842-3. Vol. 1, p. 559.

From the circumstance of cholic acid yielding these products of decomposition, we may conjecture that it is a conjugated oleic acid; and, assuming this to be the case, there remains as the adjunct the group of atoms ($C_{48}H_{39}O_9 - C_{36}H_{33}O_3 =$) $C_{12}H_6O_6$ whose per-centage composition is the same as that of the cholesteric acid found by Redtenbacher in the products of decomposition of choloidic acid, and which is therefore polymeric with it (for $C_{12}H_6O_6 : C_8H_4O_4 = 3 : 2$). That such polymeric groups of atoms frequently occur in the animal body as conjugated compounds, is obvious from Strecker's* discovery, that hippuric acid is, like the amides (see p. 36), decomposed into nitrogen, water, and an acid whose composition was found to be $C_{18}H_8O_8$, but which probably exists as a hydrate $C_{18}H_9O_9$, and in that case is polymeric with cholesteric acid. That cholic acid is oleic acid conjugated with the atomic group $C_{12}H_6O_6$ is merely a hypothetical view which, founded on certain chemical facts, may seem to indicate a direction for future experimental investigations, but cannot warrant us in advancing further in this domain of the imagination. We postpone for the present entering into the consideration of other hypotheses tending to elucidate the origin of the group of atoms conjugated with oleic acid.

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* Ann. d. Ch. u. Pharm. Bd. 68, S. 52 ff.

We must necessarily defer our remarks on the possible use of cholic acid in the animal body, till we treat of the uses of the conjugated cholic acids and of the bile generally.

NITROGENOUS BASIC BODIES.

Substances of this nature occur principally in the vegetable kingdom; those requiring a notice in animal chemistry are almost all only artificial products of known animal matters: in as far however, as they, like many of the acids which have been already described, throw much light on the constitution of the bodies from which they are derived, they must not be passed over in a work of this nature. As there exists no true alkaloid without nitrogen, the basicity of this class of bodies may be regarded as essentially depending on the amount of nitrogen which they contain; and in further confirmation of this view, we may bring forward the fact that the saturating power of these bodies is perfectly independent of the amount of oxygen which they contain. Indeed it rather depends in most cases on the amount of nitrogen; that is to say, 1 equivalent of the nitrogen of the base requires 1 equivalent of acid in order to form a neutral salt. Berzelius has, therefore, advanced the opinion that the nitrogenous bases are merely ammonia-compounds, with either a non-nitrogenous or a nitrogenous body as an adjunct. The principal argument in favour of this view is, that these bases, like pure free ammonia, cannot unite with oxygen acids, without simultaneously assimilating an atom of water, but that, on the other hand, they combine with hydrochloric and other hydrogen acids, without a separation of water: finally, they resemble ammonia in this respect, that the combination of their hydrochlorates with bichloride of platinum, are, like ammonio-chloride of platinum, difficult of solution. Moreover, that the nitrogen is not the direct cause of the basicity seems probable, from the circumstance that the saturating power of the substance, even when it contains several equivalents of nitrogen, for the most part corresponds with only one equivalent; so that only this one equivalent is to be regarded as pertaining to the ammonia, and the remainder of the nitrogen to the adjunct.

These organic bases are divisible into two tolerably well-marked groups, according as they contain or are devoid of oxygen: as the former are, without exception, volatile, and the latter not so, we might also class them as volatile and non-volatile bases.

NON-OXYGENOUS ALKALOIDS.

The bodies of this group are very similar in their empirical composition to the nitriles which we have already described: in their rational composition there can, however, be no similarity, as they are essentially different in their chemical properties. The nitriles never show any basic properties, while the alkaloids cannot be decomposed into oxygen acids and ammonia either by acids or by alkalies, nor with potassium do they form cyanide of potassium. If, therefore, Berzelius's view, that the alkaloids are conjugated ammonia, find a confirmation in any substances, it must be in the non-oxygenous alkaloids, which in all their combining relations present so many analogies with ammonia that we might regard it as the representative of this group. Even the mode of preparing certain alkaloids, as, for instance, thiosinnamine, affords evidence in favour of this view of the subject.

It is well known that, on treating cyanic acid with potash, there is a development of ammonia ($C_2NO.HO+2HO+2KO=2KO.CO_2+H_3N$); on heating cyanate of oxide of methyl or cyanate of oxide of ethyl with potash, a strongly basic alkaloid, similar to ammonia, is produced; here we feel almost compelled to assume that ammonia is formed from the cyanic acid just as from the free acid, and that this ammonia is conjugated with the carbo-hydrogen of the methyl or the ethyl, (C_2H_2 or C_4H_4,) and thus produces the alkaloid.

Urea presents perfectly similar reactions: when treated with alkalies it developes ammonia; and Wurtz* has shown that these alkaloids may be prepared in such a manner that acetate of urea, when heated with potash, shall yield the same alkaloid as is obtained by the action of potash on cyanate of oxide of methyl, namely C_2H_5N, while metacetonate of urea, similarly treated, gives the same alkaloid as is obtained by the action of potash or cyanate of oxide of ethyl, namely C_4H_7N. Although these substances may either be regarded as pertaining to the class of ethers in which the oxygen is replaced by amide, $C_4H_5.O \backsim C_4H_5.H_2N$, or as ammonia in which the third atom of hydrogen is replaced by methyl or ethyl, the most simple and probable explanation seems to be, that they should be regarded as conjugated ammonia-compounds $=C_2H_2.H_3N$, and $C_4H_4.H_3N$.

As was already mentioned, we shall here only notice those alkaloids which may be obtained from the decomposition of certain animal matters.

Many of these volatile alkaloids are liquid, like the nitriles, but most of them are crystallisable. They have generally a nauseous odour and an acrid burning taste, ar eslightly soluble or altogether insoluble in water, dissolve readily in alcohol, are most soluble in ether and in fatty and volatile oils, and react on vegetable colours. Their salts are, for the most part, crystallisable and readily soluble; but their combinations with bichloride of platinum are nearly or entirely insoluble.

ANILINE.—$C_{12}H_7N$.

Chemical Relations.

Properties.—This alkaloid forms a colourless, strongly refracting, oily fluid, with an aromatic odour; its specific gravity = 1·020, it remains fluid at—20°, evaporates very rapidly at an ordinary temperature, begins to boil at 182°, dissolves slightly in water, and in every preparation in alcohol and ether, coagulates albumen, dissolves phosphorus and sulphur, and colours Dahlia (Georgina) paper green; when exposed to the air it becomes yellow, and is converted into a resinous mass; a solution of hypochlorite of lime, on the addition of a few drops, assumes a violet colour; with nitric acid, on the other hand, aniline yields an indigo colour, and, by prolonged action, is converted into picric acid; with dilute chromic acid it yields a black or greenish blue precipitate.

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* Compt. rend. T. 38, pp. 223-227.

Composition.—According to the above formula aniline contains:

Carbon	12 atoms	77·419
Hydrogen	7 "	7·527
Nitrogen	1 "	15·054
		100·000

Its atomic weight=1162·5. According to Berzelius, aniline consists of ammonia conjugated with a carbo-hydrogen=$C_{12}H_4$.

Combinations.—Aniline forms very characteristic, and, for the most part, crystallisable salts, both with the oxygen and the hydrogen acids; in the former, but not in the latter case, the salts assimilating an atom of water.

The analogy between aniline and ammonia is further shown by the circumstance that it, like the latter, under certain conditions, may lose a portion of its hydrogen, and be converted with an acid deprived of a portion of its oxygen (and therefore with the formation of water) into combinations analogous to the amides, to which the term *anilides* has been applied. (Gerhardt.*)

As the elements of cyanate of ammonia, immediately after they are brought together, group themselves in a different manner and form urea, so cyanic acid and aniline do not form a simple salt, but a body, from which neither aniline nor cyanic acid can be again obtained, namely, aniline-urea, $C_{14}H_8N_2O_2$. (Hofmann.†)

Aniline may so assimilate cyanogen that the latter may be regarded as an adjunct, the newly-formed body, cyaniline, entirely retaining its basic properties. (Hofmann.‡)

Aniline probably affords stronger evidence than any other body yet examined in reference to this point, in favour of the substitution theory, since not merely one, but several of its equivalents of hydrogen, may be replaced by chlorine, bromine, iodine, or hyponitric acid, without the group of atoms entirely losing its basic properties. (Hofmann,[*] and Hofmann and Muspratt.[†]) Finally, a base has been discovered in which aniline is combined with the adjunct *cyanilide*, C_{12} (H_6Cy) N; to this the name of *melaniline* has been applied. (Hofmann.[‡])

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* Journ. de Pharm. et de Chim. 1845, Juill. pp. 53-56.

† Quart. Journ. of the Chem. Soc. of Lond. 1848. Vol. i., pp. 159-174.

‡ Ann. d. Ch. u. Pharm. Bd. 57. S. 247 ff.

Preparation.—This body very frequently occurs as a product of the decomposition of nitrogenous matters; thus, for instance, it is found among the products of the dry distillation of animal substances, as bone-oil (Anderson.[§]). As it had previously been obtained in various ways, it received several different names, as *cyanol*, *benzidame*, and *crystalline*, before its identity was fully established. It is most easily obtained in a state of purity by heating anthranilic acid, ($C_{14}H_6NO_3+HO=2CO_2+C_{12}H_7N$,) or phenate of ammonia, ($H_4NO.C_{12}H_5O=2HO+C_{12}H_7N$,) or from nitrobenzide and sulphuretted hydrogen, ($C_{12}H_5NO_4+6HS=6S+4HO+C_{12}H_7N$.)

Tests.—We have already pointed out the manner in which aniline reacts with hypochlorite of lime, and nitric and chromic acids; by these tests we can easily recognise it even when it is not exhibited in a perfectly pure state.

Physiological Relations.

It is remarkable that this substance, which affects the organism so unpleasantly from its smell and taste, should, according to Wöhler and Frerich's experiments,[||] be free from all poisonous action.

PICOLINE.—$C_{12}H_7N$.

Properties.—This body, which was formerly called *pyrrol*, is also a thin fluid, having a penetrating, rank, aromatic odour, and a burning bitter taste; it remains fluid at—20°, evaporates at an ordinary temperature, boils at 133°, and its specific gravity=0·955; it turns red litmus blue, does not change on exposure to the atmosphere, and does not coagulate albumen. It is not coloured by chloride of lime, and experiences no alteration from chromic acid.

Its *Composition* resembles that of aniline.

Combinations.—With acids it forms bitter tasting salts, soluble in water and alcohol, and partially deliquescent, although not so easily crystallised as those of the aniline, and less readily changed by the action of the air.

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[*] Ann. d. Ch. u. Pharm. Bd. 53, S. 40-57.

[†] Ibid. Bd. 57, S. 201-224.

[‡] Ibid. Bd. 67, S. 61-78, and Bd. 68, S. 129-174.

[§] Phil. Mag. 3 Ser., vol. 33, p. 185.

[||] Ann. d. Ch. u. Pharm. Bd. 65, S. 340.

Preparation.—This body was first discovered in coal-tar, and subsequently in the products of the distillation of bones from which the fat has been removed. (Anderson*). It is obtained by fractional distillation.

This body is isomeric, or rather identical with the *aniline* or *benzidine*$=C_{12}H_7N$ (see p. 80) obtained from nitrobenzide by ammonia and sulphuretted hydrogen; this benzidine must not be confounded with the *benzidine*$=C_{12}H_6N$, (see p. 81), which was obtained by Zinin,† from azobenzide, ammonia, and sulphuretted hydrogen.

PETININE.—$C_8H_{10}N$.

Properties.—This alkaloid is a colourless, highly refracting fluid, having a sharp pungent odour and taste; it boils at 79°, is easily soluble in water, alcohol, and ether, gives a blue tint to red litmus, is the strongest base of all these alkaloids, and is not coloured but decomposed by chloride of lime.

Composition.—According to the above formula it consists of:

Carbon	8 atoms	66·666
Hydrogen	10 „	13·890
Nitrogen	1 „	19·444
		100·000

Its atomic weight is=900·0. According to Berzelius, the theoretical formula of this body would be$=H_3N.C_8H_7$.

Combinations.—The compounds of petinine with acids are readily crystallisable, unaffected by the atmosphere, and soluble in water and alcohol. Chloride of platinum and petinine, $\overset{+}{P}.HCl.PtCl_2$ forms golden yellow crystals resembling iodide of lead, pretty soluble in cold water.

Preparation. This base is the most volatile of those yielded by the dry distillation of gelatinous tissues. It is obtained from the mixture of basic bodies and ammonia by fractional distillation.

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* Phil. Mag. 3 Ser., vol. 33, pp. 174-186.

† Journ. f. pr. Ch. Bd. 35, S. 93.

ALKALOIDS CONTAINING OXYGEN.

Few substances of this group belong to zoo-chemistry; but they are more important in reference to physiological chemistry than the non-oxygenous alkaloids which we have just considered, as they have either been found preformed in the animal body, or are able to throw considerable light on the constitution of the substances yielding them, and on organic chemistry generally. We shall therefore only consider in any detail the following substances, viz.:—creatine, creatinine, tyrosine, leucine, sarcosine, glycine, (glycocoll) urea, guanine, xanthine, taurine, and cystine; and here it will be necessary to obtain some acquaintance with the general chemical relations of all these bodies before we enter upon the consideration of each individually.

The oxygenous alkaloids do not yield in respect to their basicity to those containing no oxygen; for many of these bodies not only separate the oxides of the heavy metals from their salts but also liberate ammonia. Their basicity, however, exhibits such gradual differences that no accurate line of demarcation can be drawn between decidedly basic and indifferent nitrogenous bodies. Thus leucine and creatine are perfectly indifferent bodies, while sarcosine, which is homologous to leucine, and creatinine, which is so similar to creatine, are strongly basic; but as these indifferent bodies present a close theoretical relation to the basic bodies, or actually possess weak basic properties, we do not think that it is expedient to separate them.

There is no direct ratio between the saturating capacity of these bodies and the quantity of oxygen or even of nitrogen that they contain, for in creatinine, for instance, only the third part of the nitrogen contained in the body corresponds to the saturating capacity, while in xanthine it is the fourth, and in guanine only the fifth part. In these bodies the nitrogen may be similarly incorporated with other elements as an adjunct of the base; thus we have seen that nitrogen may be artificially added to aniline under the form of cyanogen or hyponitric acid, and that harmaline (from Peganum harmala) takes up hydrocyanic acid without changing its saturating capacity.

The greater number of the alkaloids containing oxygen are crystallisable; none are fluid at an ordinary temperature; the majority have a more or less bitter taste; not being volatile, they have no odour; all are soluble in alcohol, a few in water, and none that we have here considered, in ether; although most alkaloids act on vegetable colours, none of those under consideration, excepting creatinine and sarcosine, exhibit this property.

Their salts are almost universally crystallisable and soluble in water as well as in alcohol; with bichloride of platinum their hydrochlorates form compounds which are either insoluble or difficult of solution; their oxygen salts cannot exist without 1 equivalent of water. The most strongly basic alkaloids are precipitated by tannic acid from dilute aqueous solutions.

Although many of the substances which we shall have to consider in this group do not possess any basic properties, and therefore do not, strictly speaking, belong to it, we have arranged them together, partly on account of the analogy exhibited in their empirical composition, and partly, because in a physiological point of view, they exhibit tolerably equal values, that is to say, they are derivatives of nitrogenous tissues. The bodies which we shall now consider, are:—

Creatine	$C_8H_9N_3O_4$
Creatinine	$C_8H_7N_3O_2$
Tyrosine	$C_{16}H_9NO_5$
Leucine	$C_{12}H_{11}NO_4$
Sarcosine	$C_6H_7NO_4$
Glycine (Glycocoll)....	$C_4H_5NO_4$
Urea	$C_2H_4N_2O_2$
Xanthine	$C_5H_2N_2O_2$
Guanine	$C_{10}H_5N_5O_2$
Allantoine	$C_8H_5N_4O_5$
Cystine	$C_6H_6NS_2O_4$
Taurine	$C_4H_7NS_2O_6$

CREATINE.—$C_8H_9N_3O_4$.

Chemical Relations.

Properties.—This body forms transparent, very brilliant crystals, belonging to the clinorhombic system and containing 2 atoms of water of crystallisation; it is of a bitter, strongly pungent taste, and irritates the pharynx; it loses its 2 atoms of water at 100°, and at a higher temperature becomes decomposed; it dissolves in 74·4 parts of cold water, and in boiling water in such quantity that, on cooling, the solution becomes consolidated into a mass of delicate glistening needles; it does not dissolve in less than 9410 parts of alcohol, and not at all in ether; it does not act on vegetable colours, and forms no definite salts with acids. It dissolves in baryta-water without undergoing any change, but when boiled with it, it becomes decomposed into ammonia and carbonic acid or into *urea* and *sarcosine*. It also dissolves unchanged in dilute acids; but when heated with strong acids, it becomes converted into *creatinine*, giving off 2 atoms of water.

Composition.—This body has recently been most carefully examined by Liebig;* from whose analyses the above formula is derived, and from which we find creatine to consist of:

Carbon	.... 8 atoms	36·64
Hydrogen	.... 9 „	6·87
Nitrogen	.... 3 „	32·06
Oxygen	.... 4 „	24·43
		100·00

The 2 equivalents of water correspond to 12·08$\frac{0}{0}$ of crystallised creatine. The atomic weight of the anhydrous substance is =1637·5. Notwithstanding the various modes of decomposing creatine, no probable hypothesis can be adduced regarding its theoretical constitution. As it is almost wholly deficient in basic properties, it can hardly be regarded, according to Berzelius's view, as a conjugated ammonia; for it would in that case stand as $H_3N.C_8H_6N_2O_4$, by which the deficient basic character is made more conspicuous; while Liebig's view of regarding crystallised creatine as a combination of ammonia and 2 equivalents of glycine, (glycocoll,) ($C_8H_{11}N_3O_6 = H_3N + C_8H_8N_2O_6$,) is opposed both by the constitution of anhydrous creatine and by the deficiency in basicity. The decomposition of creatine by baryta-water into urea and sarcosine might indeed indicate that these bodies are its proximate constituents (for $C_2H_4N_2O_2 + C_6H_7NO_4 = C_8H_{11}N_3O_6$), but this is not probable; for although we know that water is expelled on the union of two organic substances, we can no more assume that urea and sarcosine are present in the dry substance, than we could maintain that oxalic acid and ammonia are contained in oxamide, or valerianic acid and ammonia in valeronitrile.

Preparation.—Creatine is obtained, according to Liebig, from finely chopped *flesh*, that has been well kneaded with water and the fluid removed by pressure. The coagulable matters are then removed by boiling, from the fluid which is thus obtained, and the phosphates by caustic baryta; during the evaporation of the fluid filtered from these precipitates the surface will be continually covered with a membranous coating which must from time to time be removed; after the fluid has been evaporated to $\frac{1}{20}$th of its volume it must be left to stand for some time, when the creatine will separate in needles. The crystals, when separated from the mother-liquid by filtering paper, must be washed with water and spirit of wine, and then again suffered to crystallise from hot water.

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* Ann. d. Ch. u. Pharm. Bd. 62, S. 257-290.

The following method is likewise given by Liebig for obtaining creatine from *urine*. The urine, after being treated with lime-water and chloride of calcium, and being filtered, is evaporated, and the greater part of the salts removed by crystallisation; the mother-liquid poured off from the crystals is then decomposed with $\frac{1}{24}$th of its weight of a syrupy solution of chloride of zinc; after some days, roundish granules of a compound of chloride of zinc and creatinine, with which some creatine is mixed, become separated; these granules, after being dissolved in boiling water, are treated with hydrated oxide of lead until there is an alkaline reaction. The fluid, after the removal of the oxide of zinc and chloride of lead by filtration, is freed from the lead and colouring matter by means of animal charcoal, and evaporated to dryness. The residue, consisting of creatine and creatinine, is treated with boiling alcohol, in which the latter dissolves readily, while the former is almost insoluble in it; by this means the two bodies can therefore be easily separated.

Tests.—In order to examine whether creatine be present in a fluid, (for which purpose a large amount of material is required,) one of the above methods should be adopted, and the properties of any creatine-like substance compared with those of pure creatine. As, however, the determination of the atomic weight is not so readily made as in the acids, an elementary analysis is indispensable for the attainment of perfect certainty.

Physiological Relations.

Occurrence.—Chevreul long since drew attention to this substance as a constituent of the decoction of flesh, but its presence was not again detected by any of the analysts who sought for it, until Schlossberger* found it in the *muscular tissue* of an alligator, and Heintz* proved its existence in beef, and was at the same time the first observer who accurately determined the composition of this body. Liebig may, however, be regarded as the first who made us thoroughly acquainted with it by his conclusive investigations regarding its chemical relations and the various situations in which it occurs. Liebig has examined so many different kinds of flesh for creatine, and so universally discovered it, that scarcely a doubt can now be entertained that creatine forms a constituent of the muscles of all the higher classes of animals. The quantity of creatine found in muscle is, however, exceedingly small. Liebig obtained only 36 grammes (consequently only 0·072%) of creatine from 100 pounds of lean horse-flesh; 30 grammes (or 0·07%) from 56 pounds of beef; but 72 grammes (=0·32%) from 47 pounds of the flesh of lean fowls; consequently for every 100 parts of flesh there were only 0·07 or at most 0·32 parts of creatine, or 1 part of creatine to 1400 parts of flesh. Liebig has further convinced himself that lean flesh contains more creatine than fat flesh; and this may probably be the cause of proportionally a large quantity of creatine being found in the tissue of the heart of the ox.

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* Ann. d. Ch. u. Pharm. Bd. 49, S. 341.

Liebig obtained the largest quantity of creatine from the flesh of fowls and martens; the quantity diminished progressively in the flesh of horses, foxes, roes, stags, hares, oxen, sheep, pigs, calves, and fishes. Liebig could frequently obtain only traces of creatine from fat flesh.

Gregory† has examined several kinds of flesh, according to Liebig's method, in reference to their amount of creatine. He found in 100 parts of bullock's heart from 0·1375 to 0·1418 parts of creatine, in the flesh of the cod-fish (*Gadus morrhua*) from 0·0935 to 0·17 parts, in the flesh of pigeons 0·0825 parts, and in the flesh of the skate (*Raja batis*) 0·0607 parts. Gregory especially recommends the flesh of the cod-fish, partly because it contains a proportionally large quantity of creatine, and partly because it most readily yields a pure, finely crystallised creatine. Sea-fish appears to contain much more creatine than fresh-water fish.

Schlossberger‡ has shown by direct experiment that human flesh presents no exception to the rule; 6 pounds of human flesh yielding about 2 grammes of creatine (therefore =0·067%).

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* Pogg. Ann. Bd. 70, S. 476-480.

† Ann. d. Ch. u. Pharm. Bd. 64, S. 100-108.

‡ Arch. f. phys. Heilk. Bd. 7, S. 209-211.

No creatine could be found in the substance of the *brain*, *liver*, or *kidneys*.

Creatine, together with creatinine, was first separated from the *urine* in the chloride of zinc compound by Heintz* and Pettenkofer† although they did not recognise its nature; Heintz‡ subsequently obtained pure creatine from the zinc compound, and employed this substance for his analysis. Liebig, however, showed that the chloride of zinc compound, as yielded by urine, contained for the most part creatinine in chemical combination, the creatine being only mixed with it.

Origin.—When we remember that creatine occurs in the decoction of flesh, and is a highly nitrogenous body, we might be led to regard it as an important nutritive agent, and as taking an active part in progressive metamorphosis. The analogy which, in its chemical relation, and in its constitution, it presents to caffeine, might moreover tend to mislead those who class that substance among nutrient bodies, from its occurrence in certain kinds of food and in certain stimulants. But this analogy is here of very little moment, for we cannot place caffeine among the nutritive agents without giving a very great latitude to the term. A substance, of which a quantity from 2 to 10 grains will produce the most violent excitement of the vascular and nervous systems—palpitation of the heart, extraordinary frequency, irregularity, and often intermission of the pulse, oppression of the chest, pains in the head, confusion of the senses, singing in the ears, scintillations before the eyes, sleeplessness, erections, and delirium,—can scarcely be reckoned among articles of nutrition even by the homœopathist, and certainly not by physiologists, when they learn how quickly caffeine becomes decomposed in the organism, and gives rise to an increased secretion of urea.

The above-named results were yielded by experiments instituted on myself and several of my pupils with pure caffeine. Five persons (one of whom was Professor Buchheim, now at Dorpat), after taking from 5 to 10 grains of this substance, were unfit for any business during the next day, while, in an experiment which I formerly made on myself, 10 grains scarcely produced any perceptible action. In all the cases there was found to be augmentation of the total amount of urea excreted in twenty-four hours.

If, however, the analogy between creatine and caffeine does not demonstrate the nutrient qualities of the former, it must be asked, whether its occurrence in a substance so nourishing as the decoction of flesh, and its large amount of nitrogen, afford more conclusive evidence in this respect? With reference to the latter, it may be assumed that nature would not suffer substances even more highly nitrogenised than creatine, as the creatinine discovered by Liebig in the urine and the urea, to escape through the kidneys, if they could be employed to further advantage in the organism, since we find so careful a providence over recognised nutrient matters, as for instance, albumen, &c., that even in disease they are only rarely found to escape with the excreta. The occurrence of creatine in the decoction of flesh affords even less evidence of its nutrient powers, for when we consider the small quantity in which it occurs in flesh, and the truly homœopathic nature of the dose which we take with the meat and broth we eat, we must regard its simultaneous appearance in the urine as a proof that its properties are not very highly esteemed in the organism, since, if they were so, this substance would probably not be discharged from the kidneys, but be retained in the same manner as albumen and gelatin. We think, however, that Liebig's complete chemical investigations of creatine, which were conducted in a manner worthy of so great a chemist, constrain us, even if unsupported by physiological proof, to regard creatine as a *product of excretion*. From its chemical qualities we regard creatine a member of the series indicating the regressive metamorphosis from the point of the highest atomic weights to bodies of the simplest composition. The readiness with which creatine becomes decomposed into creatinine, urea, and sarcosine, which is isomeric with lactamide, all of which are undoubtedly products of excretion, proves beyond a doubt, that creatine approximates more nearly to these substances than to albumen and fibrin, and indicates the great probability of creatine being decomposed even in the living body into these and other similar substances. Although such bodies as lactic acid, &c., may be employed for special purposes in the animal organism, they cannot, strictly speaking, be regarded as nutrient substances, that is to say, as materials for the renovation of nitrogenous tissues; and it is only in this light, and not in that of a supporter of heat, that we must consider creatine. Creatine is, however, a substance of the highest importance in relation to physiological chemistry, as it affords us a glimpse at the ever-recurring chemical changes which are associated with the functions of organs, and of which we have at present so little general knowledge.

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* Pogg. Ann. Bd. 62, S. 602-606.

† Ann. d. Ch. u. Pharm. Bd. 53, S. 97-100.

‡ Pogg. Ann. Bd. 62, S. 602.

CREATININE.—$C_8H_7N_3O_2$.

Chemical Relations.

Properties.—This alkaloid forms colourless, very glistening crystals, belonging to the monoclinometric system; has almost as burning a taste as caustic ammonia, dissolves in 11·5 parts of water at an ordinary temperature, but more readily in hot water; while it requires about 100 parts of cold spirit to dissolve 1 part of creatinine, it is so freely soluble in hot spirit that, on cooling, it again separates in crystalline masses; it is also slightly soluble in ether; it shows a strong alkaline action on vegetable colours, and it even separates ammonia from its salts. A moderately concentrated solution of nitrate of silver added to a solution of creatinine, causes a coagulation into a net-work of acicular crystals, which dissolve on being boiled with water, and again appear when it cools. A solution of corrosive sublimate yields a curdy precipitate, which soon becomes crystalline; chloride of zinc likewise forms a crystalline granular precipitate. Bichloride of platinum, however, yields no precipitate when the solution is somewhat dilute.

Composition.—We are indebted solely to Liebig* for our knowledge of the composition of this substance. From the analyses of its salts he deduced the above formula, according to which it consists of:

Carbon	8 atoms	42·48
Hydrogen	7 „	6·19
Nitrogen	3 „	37·17
Oxygen	2 „	14·16
		100·00

Its atomic weight=1412·5. As this body possesses such strong basic properties, we may accept the hypothesis of Berzelius regarding its theoretical composition as the most probable one, namely, that it is ammonia conjugated with a highly nitrogenous body, containing exactly 1 atom less of hydrogen than caffeine$=H_3N.C_8H_4N_2O_2$. Moreover, a comparison of the formulæ shows that creatinine contains exactly 2 atoms of water less than anhydrous creatine.

Combinations.—The combinations of creatinine with acids are, as far as is yet known, soluble in water and readily crystallisable.

Hydrochlorate of creatinine, $\overset{+}{K}.HCl$, crystallises from hot alcohol in short transparent prisms; from water, in broad leaves; with bichloride of platinum it yields an easily soluble compound which crystallises in crimson prisms $=\overset{+}{K}.HCl+PtCl_2$.

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* Ann. d. Ch. u. Pharm. Bd. 62, S. 257-290.

Sulphate of creatinine, $\overset{+}{K}.HO.SO_3$, forms concentrically grouped, transparent, square tablets, which lose no water at 100°, and remain perfectly translucent.

With the above-named *metallic salts* creatinine yields crystallisable compounds, all of which are basic double salts; with the salts of the oxide of copper it forms crystallisable double salts of a beautiful blue colour.

Preparation.—The most simple method of obtaining creatinine is from creatine, by exposing a mixture of the latter and of hydrochloric acid to evaporation, till all excess of acid is volatilised. The base is best separated from the hydrochlorate, which is thus formed, by digestion with hydrated oxide of lead. The mode of preparing creatinine from urine has been already indicated in our remarks on creatine; moreover, when it is to be prepared from the juice of flesh, the chloride of zinc compound must be employed and decomposed by hydrated oxide of lead; the creatinine may then be readily separated from the creatine by alcohol.

Tests.—This body may generally be distinguished with facility from other animal substances, when it is separated as much as possible from adherent organic substances. Its alkaline reaction, its property of forming crystalline compounds with the above-named metallic salts, the easy solubility of the compounds which it forms with bichloride of platinum and similar salts, are more than sufficient to characterise it.

Physiological Relations.

Occurrence.—It is only in the *muscles* and in the *urine* that Liebig has found creatinine. Regarding the quantity in which it exists, nothing is yet known, except that from Liebig's investigations it appears that in the muscles there is far more creatine than creatinine, while in the urine the amount of creatinine very much exceeds that of creatine.

According to Scherer* it is highly probable that the *Liquor Amnii* contains creatinine.

Origin.—From the facts which have already been communicated it can hardly be doubted that creatinine is produced from creatine; for even if Liebig had not afforded the most decisive proof, by the artificial conversion of one substance into the other, the facts that they occur in an inverse ratio in muscle and in urine, and that putrid urine yields no creatine, but only creatinine, tend to show that also, in the living body, the latter substance proceeds from the former, and consequently is to be regarded purely as a product of excretion.

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* Zeitschr. f. wissenschaftl. Zoologie. Bd. 1, S. 91.

TYROSINE.—$C_{16}H_9NO_5$.

Properties.—This body forms silky, glistening, dazzlingly white needles, is of very difficult solubility in water, and is altogether insoluble in alcohol and ether; it dissolves readily in alkaline solutions, and enters into combination with acids, with the exception of acetic acid.

Composition.—This body was discovered and analysed by Liebig.* He regards, however, a repetition of the analysis as necessary for the confirmation of the formula which he deduced.

Preparation.—Cheese, well pressed and freed from adherent butter, or well-dried fibrin or albumen, must be fused, according to Liebig and Bopp†, with an equal weight of hydrated potash, till, in addition to ammonia, hydrogen begins to be developed, or, in other words, till the original dark brown colour merges into a yellow; on then dissolving the mass in hot water, and slightly supersaturating it with acetic acid, the tyrosine separates in needles, which are obtained in a state of perfect purity by solution in potash-water and a second acidulation with acetic acid. The adherent brownish red pigment may be removed by treating the hydrochlorate of tyrosine with animal charcoal, and boiling the colourless fluid with an excess of acetate of potash; chloride of potassium is then formed, and the tyrosine, free from acetic acid, separates, on cooling, in finely matted needles. This substance is also formed, together with leucine and several acids of the first group, during the putrefaction of albumen, fibrin, and casein. Finally, since tyrosine is also formed in the decomposition of the above-named protein-compounds by concentrated hydrochloric acid or by sulphuric acid, (in which latter case leucine is also formed), this mode of procedure may also be adopted for the preparation of this substance. For this purpose we dissolve 1 part of the protein-compound in 4 times the quantity of concentrated hydrochloric acid, and then add 4 parts of sulphuric acid, and evaporate in the water-bath. The hydrochloric acid is expelled by evaporation, from the syrupy, blackish brown residue, which is then dissolved in water and boiled with milk of lime; the excess of lime is removed from the filtered fluid by sulphuric acid, whose excess is removed by acetate of lead, and the lead by sulphuretted hydrogen : in this syrup crystals of tyrosine and leucine are formed, which are separated from one another in the manner already described.

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* Ann. d. Ch. u. Pharm. Bd. 57, S. 127.

† Ibid. Bd. 69, S. 19-37.

LEUCINE.—$C_{12}H_{13}NO_4$.

Properties.—It occurs in the form of glistening, colourless leaves, which craunch between the teeth, and convey to them the sensation of a fatty matter; it is devoid of taste or odour, is lighter than water, fuses at above 100°, sublimes unchanged when carefully heated to 170°, is soluble in 27·7 parts of water at 17°·5, and in 625 parts of alcohol of 0·828 specific gravity, and in much smaller quantities of hot water and alcohol, but is insoluble in ether; it has no reaction on vegetable colours. No reagent, with the exception of nitrate of suboxide of mercury, precipitates it from its aqueous solution. It dissolves more readily in a solution of caustic ammonia than in water. It dissolves unchanged in concentrated sulphuric and hydrochloric acids, and the solution may even be warmed without the occurrence of decomposition; it dissolves unchanged in cold nitric acid, but, on boiling, is entirely converted into volatile products.

One hundred parts absorb about 28 parts of hydrochloric acid gas. Chlorine gas destroys it. On heating its aqueous solution with nitric oxide or any other oxidising agent, *leucic acid*, $C_{12}H_{11}O_5.HO$, is formed, nitrogen being developed.

If, on the other hand, it is fused with hydrated potash, there is a simultaneous formation of carbonic acid, hydrogen, and valerianate of ammonia ($C_{12}H_{13}NO_4+3KO+3HO=2KO.CO_2+H_3N+4H+KO.C_{10}H_9O_3$). It undergoes the same decomposition during the putrefaction which a solution of pure leucine very readily undergoes when a small quantity of muscular fibre or of albumen has been added.

Composition. — Mulder, following Braconnot's investigations regarding leucine, has recently analysed it, and from his analyses has deduced the formula $C_{12}H_{12}NO_4$; but still later analyses, instituted almost simultaneously by Laurent and Gerhardt,[*] by Cahours,[†] and by Horsford, indicate that in leucine there is contained 1 equivalent of hydrogen more than Mulder had assumed, and continues to assume, in his most recent investigations.[‡] Hence leucine, which, moreover, crystallises without water of crystallisation, contains:

Carbon	12 atoms	54·96
Hydrogen	13 „	9·92
Nitrogen	1 „	10·68
Oxygen	4 „	24·44
		100·00

Its atomic weight=1637·5.

Since leucine possesses scarcely any basic properties, the view that it is a conjugated ammonia$=H_3N.C_{12}H_{10}O_4$, is the least probable hypothesis regarding its theoretical composition. From Liebig's[§] experiment, to which we have already alluded, that leucine with hydrated potash yields valerianic acid besides volatile products, no theoretical formula for this body can be provisionally deduced; but Gerhardt and Laurent, as well as Cahours, have in part proved it to belong to the series of homologous bodies with the formula $C_nH_{n+1}NO_4$, to which, as we shall presently see, sarcosine and glycine pertain. But Cahours,[‖] and subsequently Strecker,[¶] availed themselves of Piria's mode of proceeding, by which he decomposed the amide-compounds by nitric oxide (see p. 36) into water, nitrogen, and the original acid, in order to obtain the above-mentioned *leucic acid* from leucine. According to this view, leucine should be regarded as *the amide* of this acid: since $H_4NO.C_{12}H_{11}O_5-2HO=C_{12}H_{13}NO_4$, the theoretical formula for this substance must be$=H_2N.C_{12}H_{11}O_4$.

Combinations.—According to Gerhardt and Laurent, leucine, in combination with acids, yields very beautifully crystallisable salts, but they bear much more the character of conjugated acids, so that we might regard leucine in itself as an adjunct; against which view, however, it may be observed that here the adjunct loses no water, as in other cases it usually does on entering into combination, and on separation takes up no water; these combinations are, however, not to be compared with the acid oxide-of-ethyl salts, since only 1 atom of acid ever combines with leucine; they are, in one respect, most similar to those ethers which may be equally represented as true neutral salts or conjugated acids, as, for instance, the salicylates of oxide of methyl and of oxide of ethyl; but still more to the compounds of the alkaloids with neutral metallic salts, such as we treated of in our remarks on creatinine.

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[*] Compt. rend. T. 27, pp. 256-258.

[†] Ibid. pp. 265-278.

[‡] Scheikund. Onderzoek. D. 5, pp. 371-377.

[§] Ann. d. Ch. u. Pharm. Bd. 57, S. 128.

[‖] Compt. rend. T. 27, pp. 265-268.

[¶] Ann. d. Ch. u. Pharm. Bd. 68, S. 52-55.

Nitrate of leucine, leuconitric acid, $C_{12}H_{13}NO_4.HO.NO_5$, separates in crystals on saturating moderately concentrated nitric acid with leucine; it has an acid but not sharp taste; the salts decrepitate on being heated, and some of them are crystallisable.

Hydrochlorate of leucine, $C_{12}H_{13}NO_4.HCl$, also crystallises readily.

Leucic acid, $C_{12}H_{11}O_5.HO$, is not only formed in the above manner by oxidising agents on leucine, but also, when an aqueous solution of this substance has been for a long time exposed to the air, it then developes a nauseous odour, and in the solution we find the ammonia-salt of this acid. It is not crystalline, but oleaginous, dissolves freely in alcohol and ether, and forms crystallisable salts with bases.

Cahours has pointed out the analogy of leucine with the base *thialdine*, discovered by Liebig and Wöhler;* both bodies containing the same equivalents of carbon, hydrogen, and nitrogen, and the 2 atoms of oxygen of the leucine being replaced by 2 atoms of sulphur in thialdine. This body is produced when aldehyde-ammonia is brought into contact with caustic ammonia and sulphuretted hydrogen; it forms large, colourless, rhombic tablets, which fuse readily, but again solidify at 42°, volatilise when exposed to the air, and can be distilled unchanged in the presence of water, but not in the dry state; they are slightly soluble in water, but dissolve readily in alcohol, and still more so in ether, and exhibit no reaction on vegetable colours. The salts that have been examined are $C_{12}H_{13}NS_4.HCl$ and $C_{12}H_{13}NS_4.HO.NO_5$; this substance also forms compounds perfectly analogous to those of leucine. On dry distillation with hydrated potash its behaviour is very different from that of leucine, since it yields leucoline (otherwise called chinoline.)

Preparation.—According to Mulder, the *caseous oxide* discovered by Proust, and Braconnot's *aposepidine*, are perfectly identical with leucine. It is principally formed in the putrefaction of casein (Iljenko* and Bopp,†) and of gluten (Walter Crum.‡) If casein, or any other albuminous body, be fused with equal parts of hydrated potash, and the tyrosine extracted from the dissolved mass in the manner already described, the leucine crystallises from the mother-liquid, and is readily purified by recrystallisation from alcohol. If gelatin be treated in a similar manner, or boiled for a long time in potash ley, we obtain leucine and glycine after saturating with sulphuric acid and removing the sulphate of potash by alcohol; and as glycine is far the less soluble of the two in alcohol, the substances may be thus easily separated from one another. Leucine is, however, also formed by the action of concentrated sulphuric or hydrochloric acid on albuminous substances; if, for instance, flesh be gently warmed with an equal volume of concentrated sulphuric acid, then boiled for nine hours with double its weight of water, the acid saturated with lime, and the residue of the filtered solution extracted with alcohol, we obtain on evaporation impure crystals of leucine, which must be purified by recrystallisation. On fusing equal parts of a protein-compound and hydrated potash, but interrupting the operation before the mass has become yellow, (as was necessary for the preparation of tyrosine,) we obtain only leucine according to the method given for tyrosine, since the latter seems to be formed from the former by prolonged action.

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* Ann. d. Ch. u. Pharm. Bd. 61, S. 1-11.

Tests.—If the leucine be obtained in a state of tolerable purity, and the properties coincide with those known to pertain to leucine, its decomposition into valerianic acid, &c., and its behaviour with nitric acid afford tolerably certain means of distinguishing it. An elementary analysis might, however, be not altogether superfluous, since it may be expected that there are a number of similar bodies for whose discovery and detailed description we may daily look.

Sarcosine.—$C_6H_7NO_4$.

Properties.—Broad, colourless, transparent plates or right rhombic prisms, acuminated on the ends by surfaces set perpendicular on the obtuse angles, melting at 100°, and subliming unchanged at a somewhat higher temperature. Sarcosine is extremely soluble in water, sparingly soluble in alcohol, and insoluble in ether; the aqueous solution has a sweetish, sharp, faintly metallic taste, has no action on vegetable colours, and is not affected by nitrate of silver or corrosive sublimate; with salts of the oxide of copper it yields the same deep blue colour as is produced by ammonia. According to Laurent and Gerhardt,* when fused with hydrated potash, it yields, like leucine, hydrogen, ammonia, and carbonic acid, but acetic in place of valerianic acid. ($C_6H_7NO_4+3KO+3HO=2KO.CO_2+4H+H_3N+KO.C_4H_3O_3$.)

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* Ann. d. Ch. u. Pharm. Bd. 58. S. 264-273.

† Ibid. Bd. 69, S. 19-37.

‡ Berzelius, Lehrb. d. Ch. Bd. 9, S. 684.

Composition.—For the discovery and analysis of this body we are also indebted to Liebig. In accordance with the above formula calculated by Liebig,† it consists of:

Carbon	6 atoms	40·45
Hydrogen	7 „	7·86
Nitrogen	1 „	15·73
Oxygen	3 „	35·96
		100·00

Its atomic weight = 1112·5.

It is worthy of remark that this body is isomeric with the *lactamide* discovered by Pelouze, (see p. 89,) and the *urethrane* prepared by Dumas from chloro-carbonic ether; hence it is the more important to ascertain the theoretical composition or the proximate grouping of the atoms in these bodies. We might take the commonly accepted view that lactamide is amide with lactic acid deprived of one atom of oxygen $=H_2N.C_6H_5O_4$, and according to the hypothesis of Berzelius, regard sarcosine as a conjugated ammonia $=H_3N.C_6H_4O_4$, which indeed is the most probable; but it is worthy of remark that lactamide, as has already been observed in p. 89, is exhibited from lactide (a body isomeric with the adjunct of ammonia in sarcosine) and ammonia; hence we should have anticipated the formation of sarcosine, but not that of an amide. The disintegration of lactamide by potash into lactic acid and ammonia, and on the other hand that of sarcosine into acetic acid, &c., would in itself be sufficient to show that these bodies were differently constituted, even if their other properties did not prove it. If, as Laurent and Gerhardt, as also Cahours,‡ expect, sarcosine is actually decomposed by nitric oxide into lactic acid, then, seeing that we are acquainted with actual lactamide, Piria's test for amide would not prove very much, and the evidence of the amide-nature of leucine and of glycine (which we are about to describe) would fall to the ground.

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* Compt. rend. T. 27, pp. 256-258.

† Ann. d. Ch. u. Pharm. Bd. 62, S. 272.

‡ Comp. rend. T. 27, pp. 265-268.

Combinations.—Sarcosine forms very crystallisable salts with several acids.

Hydrochlorate of sarcosine, $C_6H_7NO_4.HCl$, crystallises in small, transparent needles and granules; its solution, like that of the hydrochlorate of creatinine, yields no precipitate with bichloride of platinum, but on evaporation we obtain a soluble double compound. $C_6H_7NO_4.HCl+PtCl_2+2HO$, which crystallises in honey-coloured octohedral segments.

Sulphate of sarcosine, $C_6H_7NO_4.HO.SO_3+Aq.$, crystallises either in large, feathery plates, or in four-sided, strongly lustrous prisms; it is soluble in water and hot alcohol, and reddens litmus.

With *acetate of copper* sarcosine yields a deep, dark blue, double salt, which crystallises in thin plates.

Preparation.—This base has not yet been found preformed in the animal body, and is only known as a product of the decomposition of creatine, from which it is obtained in the following manner. If a boiling saturated solution of creatine be digested with pure crystallised caustic baryta, in the proportion of ten parts by weight of baryta to one part of creatine, and, after ammonia ceases to be developed, the carbonate of baryta is removed by filtration, sarcosine will separate in crystals from the filtrate; it must be purified by the precipitation of its sulphate by alcohol, and by the decomposition of this salt by carbonate of baryta.

Tests.—The mode in which it is obtained and the properties which we have described, afford sufficient evidence to identify their substance.

GLYCINE.—$C_4H_5NO_4$.

Properties.—This body which was formerly named *sugar of gelatin*, and has more recently been known as *glycocoll*, crystallises in colourless rhombic prisms belonging to the monoclinometric system, which craunch between the teeth, taste less sweet than cane-sugar, and are devoid of odour; these prisms are unaffected by exposure to the atmosphere; at 100° they lose no water; at 178° they melt and become decomposed; they dissolve in 4·3 parts of cold water, more difficultly in cold, but more easily in hot spirit of wine; they are almost insoluble in absolute alcohol and quite so in ether; these solutions have no effect on a ray of polarised light or on vegetable colours. Exposed to the action of the galvanic circuit glycine is very readily decomposed, at the negative pole there being an alkaline reaction from the separation of ammonia, while at the positive pole there is an acid reaction. Glycine dissolves unchanged in the mineral acids, and in alkaline solutions, if not too concentrated. Sulphate of copper and potash yield with glycine a deep blue solution from which no suboxide of copper separates on the application of heat. Further, on boiling glycine with a concentrated solution of potash, or with hydrated baryta or oxide of lead, the fluid developes ammonia and assumes a brilliant fiery red tint, which, however, disappears on the prolonged application of heat. In this process, in addition to the ammonia, there are formed, hydrogen, oxalic acid, and hydrocyanic acid (Horsford). If on the other hand it be fused with hydrated potash, it undergoes a decomposition analogous to that of leucine and sarcosine, into formic acid, ammonia, carbonic acid, and hydrogen gas ($C_4H_5NO_4+3KO.HO=2KO.CO_2+4H+KO.C_2HO_3$. Gerhardt and Laurent.*) If, finally, an aqueous solution of glycine be treated with nitrous acid or nitric oxide, glycic acid $=C_4H_3O_5.HO$ (Strecker,†) is formed, nitrogen gas being developed. Moreover, a non-nitrogenous acid, which in all probability is identical with glycic acid, is produced by chlorine gas and other strongly oxidising influences, as, for instance, hypermanganate, nitrate, and chlorate of potash. (Horsford.)

Horsford has analysed the baryta-salt, and deduced for the acid the formula $C_3H_3O_6$, but the analysis yielded less hydrogen and more carbon than are represented by this formula; if Horsford had accidentally omitted to calculate for the organic substance the carbonic acid retained in the baryta, the formula of the baryta-salt would be $=BaO.C_4H_3O_5$, and consequently would correspond with that of Strecker's acid. The baryta-salt was somewhat insoluble, but crystallised well.

Composition.—According to the above formula which is deduced from the coincident analyses of Laurent,‡ Mulder,§ and Horsford, free glycine, dried at 100°, consists of:

Carbon	4 atoms	32·00
Hydrogen	5 "	6·67
Nitrogen	1 "	18·67
Oxygen	3 "	42·66
		100·00

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* Compt. rend. T. 27, pp. 256-258.

† Ann. d. Ch. u. Pharm. Bd. 68, S. 54.

‡ Compt. rend. T. 20, p. 789.

§ Journ. f. pr. Ch. Bd. 28, S. 294-297.

Its atomic weight=937.5. Horsford,[*] who has recently made the most complete investigation regarding this substance, is led, from a consideration of its compounds with acids, as well as with certain metallic oxides, to assign to free glycine the formula $C_4H_4NO_3.HO$, regarding it as containing 1 atom of combined water; thus throwing doubts on the homology of leucine, sarcosine, and glycine, maintained by Laurent and Cahours. The analogy in the constitution of these three bodies is undeniable; independently of the fact that the empirical formula $C_nH_{n+1}NO_4$ is also applicable to hydrated glycine, its relation towards hydrated potash as well as towards nitric oxide, indicates its extreme similarity to the two other bodies. Strecker's discovery that glycic acid is produced when glycine is decomposed by nitric oxide would lead to the inference that glycine is the amide of glycic acid, just as leucine might be regarded as the amide of leucic acid. Berzelius[†] assumes for glycine double the above atomic weight, and hence he writes its empirical formula=$C_8H_8N_2O_6+2HO$; theoretically he regards it as an alkaloid, namely, as ammonia conjugated with a nitrogenous body, so that its rational formula is $H_3N.C_8H_5NO_6+2HO$.

Here, indeed, the homology with sarcosine entirely fails. Berzelius bases his view regarding the establishment of the doubled atomic weight on the strong acidity of the salts containing 1 atom of this acid, $C_4H_4NO_3$; but in such weak basic bodies, little stress should be laid on this acidity, while, moreover, the compound of glycine with salts, and especially with chlorides, entirely supports the atomic weight assigned by Horsford. It is chiefly from the behaviour of glycine when acted on by the galvanic current that Horsford is inclined to regard it as a salt-like compound, namely, as a compound isomeric with the hypothetical anhydrous fumarate of ammonia, since $C_4H_4NO_3=H_3N+C_4HO_3$. Probably, however, Laurent and Strecker's hypothesis still holds good, since, in organic nature, we much more frequently meet with amide-compounds than with compounds of anhydrous acids with ammonia.

Combinations.—All the combinations of glycine with acids are crystallisable, of tolerably easy solubility, and have a strong acid reaction.

Neutral hydrochlorate of glycine, $C_4H_4NO_3.HO.HCl$, crystallises in long flat prisms which are transparent and glistening, soon deliquesce when exposed to the atmosphere, and dissolve readily in water and in spirit of wine, but slightly in absolute alcohol.

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[*] Ann. d. Ch. u. Pharm. Bd. 60, S. 1-57.

[†] Jahresber. Bd. 27, S. 655.

Horsford has prepared the following basic hydrochlorates:— $2C_4H_4NO_3+HO+HCl$, rhombic prisms not affected by the atmosphere; $2(C_4H_4NO_3.HO)+HCl$, which crystallises well; $3C_4H_4NO_3+2HO+2HCl$ was obtained from dry glycine in hydrochloric acid gas; in a similar way the same salt was obtained with only 1 atom of water; these basic salts might possibly be mixtures of two salts. Berzelius* obtained a combination of hydrochlorate of glycine and *bichloride of platinum*, by extracting a mixture of these two compounds with absolute alcohol, and then precipitating the excess of hydrochlorate of glycine from the solution by ether; the double compound which he thus obtained, occurred in the form of yellow, oily drops, which when exposed to the air crystallised in yellow needles like wavellite; this compound is easily soluble in water and in alcohol, and contains much water of crystallisation, in which respects it is very different from the analogous double compounds of most of the alkaloids. If, however, free glycine be mixed with bichloride of platinum, a compound is formed which is represented by $C_4H_4NO_3+2HO+PtCl_2$, and occurs in black (Berzelius) or red crystals, (Horsford.) The following compounds with sulphuric acid were obtained by Horsford: $C_4H_4NO_3.SO_3$; $C_4H_4NO_3.HO.SO_3$; $3(C_4H_4NO_3.HO)+2(SO_3.HO)$; $3C_4H_4NO_4+2SO_3+HO$; $3(C_4H_4NO_3.HO)+2SO_3+HO$.

Nitrate of glycine, $C_4H_4NO_3.HO+NO_5.HO.$, usually occurs in the form of acicular crystals, but sometimes as large tabular crystals of the monoclinometric system; these crystals are unaffected by exposure to the atmosphere and have an acid taste.

Nitrate of glycine was formerly regarded as a conjugated acid, but these compounds which result from the union of nitrate of glycine with bases, are true nitrates, since, as Horsford has shown, they are directly produced on digesting the nitrates with glycine.

Oxalate of glycine, $C_4H_4NO_3.HO.C_2O_3$, occurs in wavellite-like crystals which are unaffected by exposure to the atmosphere.

Acetate of glycine, $C_4H_4NO_3.HO.C_4H_3O_3+2HO$, is crystallisable, and insoluble in alcohol.

Horsford further observed that glycine formed crystallisable compounds with many salts, (similar to that which it forms with bichloride of platinum,) most of which contain 1 atom of glycine to 1 atom of the salt. With *bases*, especially with hydrated baryta and potash, crystallisable compounds are also formed. *Protoxide*

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* Jahresber. Bd. 27, S. 658.

of copper-glycine was obtained by Boussingault, and found to be represented by the formula $C_4H_4NO_3.CuO$; Horsford found 1 atom of water, in this compound which crystallised in brilliant blue needles. Similarly to the hydrated oxide of copper, the hydrated oxide of lead, and oxide of silver, may be dissolved in an aqueous solution of pure glycine, and the compound after being precipitated by the addition of alcohol, may be obtained in a crystalline form. The *lead-compound* crystallises in prisms, the *silver-compound* in wart-like masses.

There is much regarding these compounds that still remains to be investigated; we have, however, entered more fully into the subject of their composition than we should otherwise have done, because it is on this point that we must form our judgment respecting the constitution of glycine, and decide in favour of one or the other of the above hypotheses.

Preparation.—Glycine has not yet been found in an isolated state in the animal body: there is, however, reason for believing that this substance is contained preformed as an adjunct in certain known animal acids; moreover, the relations of this body towards acids, bases, and salts, (which we have already described,) support this view; while, in many cases with which we shall become acquainted as we proceed, it is more than probable that glycine is formed on the separation of the acid from its proper adjunct, as glycerine is produced in the saponification of the hypothetical oxide of lipyl. As instances, we may mention hippuric and glycocholic acids; and when we treat of these acids, we shall enter into the physiological relations and the genesis of glycine.

It has long been known that glycine is a product of the decomposition of animal substances, especially of gelatin, by the action of concentrated mineral acids or caustic alkalies. The following is the best method of obtaining it from gelatin. If the gelatin be boiled with a strong solution of potash till ammonia ceases to be developed, it becomes entirely decomposed into a mixture of 4 parts of glycine and 1 of leucine; the fluid neutralised with sulphuric acid is evaporated to dryness, and the residue extracted with spirit of wine which dissolves both the glycine and the leucine; the glycine as being the least soluble in alcohol, crystallises first, while the leucine subsequently crystallises; by recrystallisation and treatment with a little animal charcoal, the glycine can be obtained perfectly pure.

The method of obtaining glycine from hippuric acid is even simpler; for if 1 part of this acid be boiled for half an hour with

4 parts of concentrated hydrochloric acid, it becomes decomposed into glycine and benzoic acid ; on the addition of water to the boiled fluid, a great part of the benzoic acid separates and must be removed by filtration ; the clear fluid is then evaporated nearly to dryness, and the residue (hydrochlorate of glycine) decomposed with caustic ammonia ; finally the glycine is precipitated by, and washed with, absolute alcohol.

Tests.—When the substance suspected to be glycine is separated as much as possible from all other matters, the most striking of the properties by which it may be distinguished are its relation towards a hot solution of potash, its difficult solubility in alcohol, and the blue solution which it yields with caustic potash and sulphate of copper, without any separation of the suboxide; and if, further, we study its power of combining with acids as well as with baryta, oxide of copper, oxide of lead, &c., and forming crystallisable bodies, there can hardly remain any doubt regarding its nature. It may easily be distinguished from leucine by the form of its crystals and by its becoming decomposed on exposure to heat.

According to Horsford the quantities of urea and uric acid in the urine are increased after the ingestion of glycine, but no unchanged glycine is found in the urine.

UREA.—$C_2H_4N_2O_2$.

Chemical Relations.

Properties.—Urea crystallises, when it separates rapidly, in white, silky, glistening needles; but when the crystallisation is effected slowly, in flat, colourless, four-sided prisms full of cavities and appearing to be formed of numerous parallel crystalline lamellæ: at the ends the prism is terminated by one or two oblique surfaces. According to C. Schmidt*, these forms do not pertain to the monoclinometric system, but rather to a hemihedral form belonging to the rhombic system, and bounded by parallel surfaces. These crystals contain no water. Urea is devoid of smell, of a saltish, cooling taste, and is unaffected by exposure to the atmosphere; it dissolves readily in its own weight of water, giving rise to a marked evolution of heat; in hot water it dissolves in every proportion; it is also soluble in 4 or 5 parts of cold and in 2 parts of warm alcohol; it is insoluble in ether, if anhydrous and devoid of alcohol, and in etherial oil, and exerts no action on vegetable colours. Its concentrated aqueous solution is not changed by boiling or by long keeping, but a dilute solution suffers change.

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* *Entwurf* u. s. w. S. 41.

At about 120° urea fuses without suffering change, but at a little above that temperature it begins to develope ammonia, to become pulpy, and to change into cyanuric acid ($3C_2H_4N_2O_2 = 3H_3N + C_6HN_3O_4.2HO$); when rapidly heated it also yields cyanic acid which is produced from the previously formed cyanuric acid ($C_6HN_3O_4.2HO = 3C_2NO.HO$). On heating urea very slowly, it becomes converted (according to Wöhler and Liebig[*]) into a glistening white body, insoluble in water but soluble in acids and alkalies, carbonic acid and ammonia being evolved during the process. This body $= C_4H_6N_4O_2$, for $3C_2H_4N_2O_2 - (2CO_2 + 2H_3N) = C_4H_6N_4O_2$. If, on the other hand, urea be kept for some time in a state of fusion at from 150° to 170°, not only are the above-named compounds formed, but also (according to Wiedemann[†]) the *biuret*, $C_4H_5N_3O_4$, whose production is explained by the equation, $2C_2H_4N_2O_2 - H_3N = C_4H_5N_3O_4$.

If chloride of sodium or hydrochlorate of ammonia be present in a solution of urea, the former will crystallise in octohedra and the latter in cubes; if, however, the crystals be again dissolved in water, and allowed to crystallise anew, they separate in the ordinary manner, namely, the chloride of sodium into cubes, and the hydrochlorate of ammonia into octohedra or feathery forms.

Urea will combine only with certain acids and a few bases; neither the metallic salts, tannic acid, nor any other re-agent, can precipitate it from its solutions.

On heating a concentrated solution of urea with nitrate of silver, cyanate of silver separates, while nitrate of ammonia remains in solution. ($C_2H_4N_2O_2 + AgO.NO_5 = AgO.C_2NO + H_3N.HO.NO_5$).

By nitrous acid urea is decomposed into nitrogen, water, and carbonic acid; ($C_2H_4N_2O_2 + 2HO + 2NO_3 = 6HO + 2CO_2 + 4N$;) by chlorine into nitrogen, carbonic acid, and hydrochloric acid; ($C_2H_4N_2O_2 + 2HO + 6Cl = 6HCl + 2CO_2 + 2N$.)

On boiling urea either with strong mineral acids or with caustic alkalies, it takes up 2 atoms of water and is decomposed into ammonia and carbonic acid ($C_2H_4N_2O_2 + 2HO = 2H_3N + 2CO_2$.)

If organic matters, either putrefying or capable of undergoing putrefaction, be mixed with an aqueous solution of urea, the latter is soon converted into carbonic acid and ammonia.

[†] Ann. d. Ch. u. Pharm. Bd 54, S. 371.

[‡] *Journ. f. pr. Ch.* Bd. 43, S. 271-280.

Composition.—According to the above formula urea consists of:

Carbon	....	2 atoms	....	20·000
Hydrogen	....	4 "	....	6·666
Nitrogen	....	2 "	....	46·667
Oxygen	....	2 "	....	26·667
				100·000

Its atomic weight=750·0. Although there have been many discussions regarding the rational constitution of urea, much still remains to be cleared up. Dumas, after his discovery of oxamide, started the hypothesis, that urea is an amide of carbonic acid, since $2H_3N + 2CO_2 - 2HO = C_2H_4N_2O_2$, and the relation of urea towards nitrous acid, and its ready decomposition into carbonic acid and ammonia, seem to support this view. But Berzelius justly points out the analogy, in their combining relations with acids, between the alkaloids and urea, and regards the latter as ammonia conjugated with a nitrogenous body which he names *urenoxide*, so that the rational formula for urea would be $= H_3N.C_2HNO_2$. Independently of the analogy between the salts of urea with those of the alkaloids, the following consideration mainly supports this view: cyanate of ammonia$=H_3N.HO.C_2NO$, is convertible, as we shall presently see, into urea; the grouping of the atoms in urea must be perfectly different from that in this salt, since urea has lost all the properties of a salt. But we know that free hydrated cyanic acid is spontaneously converted by a transposition of its atoms into the so-called *cyamelide*$=C_2HNO_2$; now, nothing is more obvious than to assume that in the combination with ammonia the cyanic acid becomes incorporated with the water of the ammonia-salt, in the same manner as in the free state, and that this cyamelide, if not identical with, is highly analogous to the urenoxide of Berzelius, and thus forms the adjunct of the ammonia in urea. Probably, also, the existence of the biuret might be made available in the support of this hypothesis, since the most simple view of the biuret is to regard it as consisting of 2 atoms of urenoxide and 1 atom of ammonia, for $C_4H_5N_3O_4 = H_3N + 2C_2HNO_2$.

Combinations.—It is only with some acids that urea has a tendency to combine. Cap and Henry* fancied that they had prepared compounds of urea with sulphuric, lactic, hippuric, and uric acids, but the existence of those compounds is very correctly doubted. We know with certainty only three salts of urea, namely, the hydrochlorate, the nitrate, and the oxalate.

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* Journal de Pharm. T. 25, p. 133.

Hydrochlorate of urea, $C_2H_4N_2O_2.HCl$, was simultaneously obtained by Erdmann[*] and Pelouze[†]. They prepared it by passing a stream of dry hydrochloric acid gas over urea. The compound is white and hard, and crystallises in plates; it attracts water from the atmosphere, and from this water the hydrochloric acid escapes by evaporation, and pure urea crystallises; in water the salt becomes rapidly decomposed into hydrochloric acid and urea.

Nitrate of urea, $C_2H_4N_2O_2.HO.NO_5$ (according to the analysis of Regnault, which has been repeated by Marchand[‡], Heintz[§], Fehling,[||] and Werther,[¶]) is formed by mixing a concentrated solution of urea with an excess of nitric acid; the compound at once separates (on cooling, almost perfectly,) in large nacreous, shining scales, or in small, glistening, white plates; on examining under the microscope the contact of the urea and the nitric acid, we first observe very obtuse rhombic octohedra, at whose acute angles ($=82°$) more particles are gradually accumulated, so that they appear to increase in size, and the octohedra become converted into rhombic tablets, or form hexagonal tablets (whose opposite acute angles likewise are 82°); these crystals always occur isolated, or in uniformly superimposed masses (C. Schmidt[**]). This salt is uninfluenced by the atmosphere, has an acid taste, is more soluble in pure water than in water containing nitric acid, and dissolves in alcohol, producing considerable depression of temperature; on evaporating its aqueous solution, the salt very readily effloresces; it reddens litmus; a concentrated solution is not affected by boiling, but a dilute solution is converted into carbonic acid, carbonate of ammonia, water, and nitrous oxide ($C_2H_4N_2O_2.HO.NO_5=H_3N+2CO_2+2HO+2NO$). On heating dried nitrate of urea rapidly, it decrepitates, but on heating it slowly to 140°, it becomes decomposed into carbonic acid, nitrous oxide, urea, and nitrate of ammonia. If the solution of this salt be not too dilute, a solution of oxalic acid precipitates oxalate of urea.

Oxalate of urea, $C_2H_4N_2O_2.HO.C_2O_3$ (sometimes, according to

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[*] Journ. f. pr. Ch. Bd. 25, S. 506.

[†] Ann. de Ch. et de Phys. 3 Sér. T. 6, p. 63.

[‡] Journ. f. pr. Ch. Bd. 35, S. 481.

[§] Pogg. Ann. Bd. 66, S. 114-122.

[||] Ann. d. Ch. u. Pharm. Bd. 55, S. 249.

[¶] Journ. f. pr. Ch. Bd. 35, S. 51-66.

[**] Entwurf u. s. w. S. 42-45.

Marchand, taking up 2 atoms of water of crystallisation) is also obtained by the direct union of the constituent parts, and forms, as far as the unaided eye can perceive, long thin plates or prisms; under the microscope it is usually seen in hexagonal plates, similar to those of nitrate of urea, interspersed occasionally with four-sided prisms with planes of truncation proceeding from the broader sides of the rectangular section. The form of this oxalate, like that of the nitrate of urea, belongs to the monoclinometric system. This salt has an acid taste, dissolves at 16° in 22·9 parts of water and in 62·5 of alcohol; it is precipitated from its aqueous solution by an excess of oxalic acid. On exposure to heat it is decomposed into carbonate of ammonia and cyanuric acid.

Like glycine, urea also unites with *salts*, which hold it in such firm combination, that not only does no decomposition ensue when their solutions are boiled, but even oxalic and nitric acids fail to separate the urea from some of their compounds (Werther*).

On mixing concentrated solutions of urea and nitrate of silver, there are formed thick prisms with a rhombic base which are readily soluble in water and alcohol$=C_2H_4N_2O_2.AgO.NO_5$. On the addition of a solution of soda to the solution of these crystals, a yellow precipitate is obtained$=5AgO+2C_2H_4N_2O_2$. Besides these, Werther has also obtained the following combinations:—$C_2H_4N_2O_2+2AgO.NO_5$; $CaO.NO_5+3C_2H_4N_2O_2$; $MgO.NO_5+2C_2H_4N_2O_2$; $NaO.NO_5+C_2H_4N_2O_2+2HO$; $NaCl+C_2H_4N_2O_2+3HO$, crystallising in deliquescent rhombic prisms; $2HgCl+C_2H_4N_2O_2$, flat prisms glistening like mother-of-pearl. Urea cannot be separated from the solutions of these compounds either by nitric or oxalic acid.

Products of its metamorphosis.—Biuret, $C_4H_5N_3O_4$, is, as we have already mentioned, the chief product (together with cyanuric acid) which is obtained on heating pure urea or its nitrate to a temperature of 152°—170°; the cyanuric acid is precipitated by basic acetate of lead from the aqueous solution of the fused product, and the excess of lead removed by sulphuretted hydrogen; the biuret is then obtained by the evaporation of the solution. It forms small crystal which dissolves readily in water, and still more readily in alcohol; it exerts no action on vegetable colours, does not combine with bases, and dissolves unchanged in concentrated sulphuric and nitric acids; with sulphate of copper and potash it yields a red solution. Its rational formula$=H_3N+2C_2HNO_2$.

Preparation.—Urea not only occurs preformed in the animal body, but can also be artificially prepared. When Wöhler made the beautiful discovery that urea was formed by the union of cyanic acid and ammonia, the physiologists of that day who were still imbued with ideas of vital forces, were astonished that a matter which appeared only capable of formation by organic force, could also be formed by the hand of the chemist from so-called inorganic matters. The astonishment of the physiologists has, however, gradually ceased, not only because they have for the most part shaken off their adherence to irrational vital forces, but also because since that time many other substances have been artificially produced, which are identical with, or at all events most similar to previously known organic matters. We have learned to regard urea as one of the most common products of decomposition, not only of natural organic bodies, but also of artificial substances. It would occupy too much of our present space, were we to enumerate all the cases in which urea occurs as a product of the decomposition of a nitrogenous substance; we will here only mention its formation on the union of cyanogen and water, of fulminate of copper and hydrosulphate of ammonia (Gladstone*), in the decomposition of allantoine by nitric acid, of creatine by the alkalies, of alloxan by a boiling solution of acetate of lead, &c.

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* Journ. f. pr .Ch. Bd. 35, S. 51-66.

There are various ways in which urea may be obtained from urine, but it is chiefly effected by nitric or oxalic acid; it is more advisable to use the alcoholic extract of urine than the residue left by its direct evaporation; if nitric acid be used, the nitrate of urea must be exposed to due pressure between tiles and filtering paper, and after it has been dissolved in a little water, must be decomposed with carbonate of lead or of baryta; crystals of nitrate of lead or baryta soon separate from the filtered fluid, which must be evaporated and extracted with alcohol; this alcoholic solution may contain, in addition to urea, a little nitrate of lead, but it takes up no nitrate of baryta; when baryta has been used, the alcoholic solution must be decolorised with animal charcoal; when the salt of lead has been used, the solution is often perfectly colourless after the precipitation of the metal by sulphuretted hydrogen. The urea separates in a crystalline form, on the evaporation of the alcoholic solution.

In order to prepare urea from cyanate of ammonia, we raise a mixture of 28 parts of ferrocyanide of potassium, from which all the water has been expelled, and 14 parts of well-dried, good peroxide of manganese, to a faint red heat; (even when the mixture is sufficiently heated at a single spot, the whole mass assumes a phosphorescent appearance;) from this glowing residue the cyanate of potash which has been formed must be extracted with cold water, and mixed with 20½ parts of dry sulphate of ammonia; most of the sulphate of potash separates in a crystalline form, while the cyanate of ammonia, now converted into urea, remains in solution. The remaining sulphate is separated by crystallisation, but more perfectly by alcohol.

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* Ann. d. Ch. u. Pharm. Bd. 66, S. 1-5.

Tests.—Urea may generally be very easily recognised by its properties, especially by its behaviour towards nitric and oxalic acids; but when we have to discover very minute quantities of this substance in albuminous fluids, it is often very difficult to determine its presence with scientific precision. It is in alcoholic extracts that we must always seek for urea, but before we proceed to search for it, there are several precautionary measures to be adopted, the neglect of which would render our attempt to discover it futile. In the first place, in reference to the presence of albuminous substances, if we wish to discover small quantities of urea in albuminous fluids, we must not be satisfied with the removal of the albumen by simple boiling; since by the coagulation of the albumen the fluid becomes more alkaline, and might, during evaporation, induce a decomposition of the urea; moreover, all albuminous matter is not precipitated by boiling, but a portion remains dissolved by the alkali, and is taken up in the alcoholic extract; on evaporation this albumen undergoes a change which probably coöperates with the alkali in inducing the decomposition of the urea. This may explain how it was that Marchand could only recover 0·2 of a gramme of urea from a mixture of 200 grammes of serum and 1 gramme of urea. Hence, before boiling the albuminous fluid, we must add a few drops of acetic acid, so as to give it a slightly acid reaction, whereby not only is the alkalescence of the fluid prevented, but a much more perfect separation of the coagulable matters is effected. If the residue of the fluid from which the coagulated matters have been filtered be extracted with cold alcohol, and the solution rapidly evaporated, so as to cause the chloride of sodium (taken up by the cold alcohol) to separate as much as possible in crystals, on then bringing a drop of the mother-liquid in contact with nitric acid under the microscope, we shall observe the commencement of the formation of the rhombic octohedra, and the hexagonal tablets, in which, if the investigation is to be unquestionable, the acute angles (=82°) must be always measured. After the determination of the nitrate we may also obtain the oxalate, and submit it to microscopic examination. A good crystallometric determination yields, however, the same certainty as an elementary analysis which, in these cases, would never, or extremely seldom, be possible.

Formerly the presence of small quantities of urea was supposed to be established when chloride of sodium crystallised in the octohedral form; but independently of the circumstance that other substances besides urea may induce a similar action on the form of the crystals of this salt, it must be borne in mind that chloride of sodium, when we trace the formation of its crystals under the microscope, presents itself in combinations of the regular system, with a complexity varying with the minuteness of the crystals. This occurs when we allow pure chloride of sodium to crystallise; and it is still more the case when organic matters are mixed with the solution. I am acquainted with no other substance of the regular system which presents such uncommon crystals under the microscope as chloride of sodium. We need only expose the alcoholic extract of any animal fluid to spontaneous evaporation, in order to recognise with the naked eye, in the greater crystals, the combinations which we have perceived on examining the crystallisation of a solution of pure salt under the microscope.

In order to determine the *amount* of urea in urine, most analysts have followed the method proposed by Mitscherlich,* and have availed themselves of the insolubility of the nitrate. There are several causes of error in this method which cannot be altogether avoided, but with due care may be made very inconsiderable. They chiefly consist in the imperfect insolubility of this salt, and on the adherence of the so-called extractive matters to it; if, however, we use an excess of nitric acid for the purpose of separating the urea, cool the fluid artificially, filter after some time, rinse the salt with cold nitric acid, and, after it has been submitted to pressure, dry it at a temperature not exceeding 110°, we shall not have so great a loss of urea as Heintz† maintains must always occur in adopting this method; but in relation to accuracy, the results fall far short of those obtained in the determination of mineral substances. The idea occurred almost simultaneously to Ragsky‡ and Heintz§ that the urea in urine might be determined quantitatively by its decomposition by *sulphuric acid.* Both investigators have satisfied themselves that the so-called extractive matters of the urine do not modify the result of the experiment; the essential point in this method, which is somewhat more complicated, but doubtless more accurate than that by nitric acid, consists in our determining, by means of bichloride of platinum, the amount of potash and ammonia (if the latter be present) in a specimen of urine, and in our then treating a second specimen with sulphuric acid, and gradually heating it to 180° or 200°, or as long as any effervescence continues; the fluid is then filtered, and the amount of ammonia determined by bichloride of platinum; deducting from the precipitate thus obtained that which was yielded by the other specimen (corresponding to the potassio-chloride of platinum,) we can easily calculate the amount of urea from the ammonio-chloride of platinum, or from the platinum itself left on the incineration of the residue.

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* Pogg. Ann. Bd. 31, S. 303.
† Ibid. Bd. 66, S. 114-160.
‡ Ann. d. Ch. u. Pharm. Bd. 56, S. 29-34.
§ Pogg. Ann. Bd. 68, S. 393-410.

A still better method, by which urea may be determined quantitatively, although not perfectly free from error, has been given by Millon.* It is based on the fact that urea is decomposed by nitrous acid into nitrogen and carbonic acid; to effect this object a solution of nitrite of suboxide of mercury is dissolved in nitric acid, and added to a weighed portion of urine; on warming this mixture there is a development of nitrogen and carbonic acid, which latter gas is caught in a potash-apparatus and weighed. Some of the extractive matters might yield carbonic acid, even if none of the other constituents of the urine did so; this, however, is denied by Millon. It must also be recollected that the urine always contains free carbonic acid in solution.

Finally, a method has been proposed by R. Bunsen† for the quantitative determination of urea, founded on the property that its solutions *undergo decomposition in closed vessels at a temperature of from* 120° *to* 240°; the carbonic acid which is thus formed is combined with baryta, and the amount of urea is calculated from that of carbonate of baryta.

Physiological Relations.

Occurrence.—Urea is one of the principal products of excretion of the kidneys: hence it chiefly occurs in the urine. Although it constitutes the greatest part of the solid constituents of the urine, it is contained in the liquid urine in very variable quantities in consequence of the physiological relations, in accordance with which the amount of water in the urinary secretion varies in so extraordinary a degree. In order to convince ourselves of the quantity of urea excreted in the urine, we must examine the urine collected in a definite interval in relation to its proportion of urea. As, in the consideration of "Urine," we shall return to this subject, we will here only remark that the urine of a healthy man contains generally from 2·5 to 3·2% of urea, that the ratio of urea to the other solid constituents is about=9 : 11 or 7 : 9, and that a healthy man in twenty-four hours excretes from 22 to 36 grammes.

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* Compt. rend. T. 26, pp. 119-121.

† Ann. d. Ch. u. Pharm. Bd. 65, S. 375-387.

My experiments* show that the amount of urea which is excreted is extremely dependent on the *nature of the food* which has been previously taken. On a purely animal diet, or on food very rich in nitrogen, there were often two-fifths more urea excreted than on a mixed diet; while, on a mixed diet, there was almost one-third more than on a purely vegetable diet; while, finally, on a non-nitrogenous diet, the amount of urea was less than half the quantity excreted during an ordinary mixed diet.

In my experiments on the influence of various kinds of food on the animal organism, and especially on the urine, I arrived at the above results, which in mean numbers may be expressed as follows: on a well regulated mixed diet I discharged, in 24 hours, 32·5 grammes of urea, (I give the mean of 15 observations); on a purely animal diet 53·2 grammes (the mean of 12 observations); on a vegetable diet 22·5 grammes (the mean of 12 observations); and on a non-nitrogenous diet 15·4 grammes (the mean of 3 observations).

It is especially worthy of remark, that the augmentation of the urea in the urine occurs very soon after the use of highly nitrogenous food, and that in such cases often five-sixths of the nitrogen taken in the food in 24 hours are eliminated as urea by the kidneys.

When I took 32 boiled hens' eggs daily, I consumed in them about 30·16 grammes of nitrogen, but in the above-mentioned quantity of urea I discharged only about 25 grammes in 24 hours. On the morning following the day on which I had taken only flesh or eggs, the urine was so rich in urea that immediately on the addition of nitric acid it yielded a copious precipitate of nitrate of urea; hence Prout's assertion may be correct in reference to England, that freshly passed urine often gives a precipitate of nitrate of urea immediately on the addition of nitric acid, although on the continent, where less animal food is taken, no one, so far as I know, has made a similar observation; and hence also the urine of carnivorous animals is very rich in urea (Vauquelin*, Hieronymi†, Tiedemann and Gmelin‡,) while the urine of graminivorous animals is comparatively poor in this constituent (Boussingault§).

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* Journ. f. pr. Ch. Bd. 25, S. 22-29, and Bd. 27, S. 257-274.

Notwithstanding the considerable influence which the nature of the food exerts on the quantity of urea excreted by the kidneys, there is as much urea in the urine after prolonged abstinence from all food (after a rigid fast of 24 hours) as after the use of perfectly non-nitrogenous food.

Lassaigne‖ found urea in the urine of a madman who had taken no food for 14 days; and we observe something similar almost daily in patients with typhus fever and other diseases, who for 14 days or more have taken nothing but an oily emulsion or an emollient decoction, and yet always pass urine containing urea, and often rich in it. After living for three days on a perfectly non-nitrogenous diet, I still found, in the morning urine, more than 1% of urea.

Strong *exercise* of the bodily powers causes an increased excretion of urea.

While, from numerous observations, I ascertained that, during my ordinary habits of life, I discharged about 32 grammes in 24 hours, I found that after strong bodily exercise, I, on one occasion, passed 36 grammes, and on another 37·4 grammes in 24 hours.

The urine of women and children contains, according to Becquerel,¶ less urea than that of men.

Becquerel found the ratio of urea excreted in 24 hours by women, to that excreted by men=15·582 : 17·537.

Like Becquerel, I have failed in establishing the fact that there is an augmentation of urea in certain forms of disease, although English physicians have shown an inclination to assume an urea-diathesis.

Although we are, *à priori,* prejudiced against all these diatheses which English physicians have attempted to establish on certain urinary analyses, (see p. 47,) we must especially protest against such an urea-diathesis; for how does this indicate a morbid process? The nature of this or that disease does not depend on an increased excretion of urea, which is only a consequence of another process.

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* Schweigg. Journ. Bd. 3, S. 175.

† Journ. de Ch. et de Pharm. T. 3, p. 322.

‡ Verdauung u. s. w. Bd. 2, S. 4.

§ Ann. de Chim. et de Phys. 3 Sér. T. 15, pp. 97-114.

‖ Journ. de Chim. méd. T. 1, p. 272.

¶ Séméiotique des Urines &c. Paris, 1841, p. 34.

The urea is possibly only excreted in increased quantity when material for its formation is sufficiently supplied; now if polyphagia be not combined with this urea-diathesis, the source of the urea must be sought in the waste or consumption of the nitrogenous tissues; this is not based on the tendency of the tissues to be converted into urea, but depends on other processes which accompany many morbid processes. In diseases where such a consumption actually occurs, I have never found the urea passed in twenty-four hours exceed the normal quantity, and have very often found it far beneath the average.

A diminution in the amount of urea excreted during disease in twenty-four hours is very frequently observed: this, however, in most cases, may be dependent on the low diet.

Becquerel has made the best observations in reference to this subject; it appears, however, to us, that such investigations may rather serve to enable us to form an opinion of the morbid process in a special case, than to establish general rules regarding the diminution of the urea in the urine in certain classes of disease.

It is by careful observation of the urine in individual cases, and not by drawing general inferences, that we can make these examinations useful.

Many chemists have long sought in vain to detect urea in *normal blood;* Simon believed that he had found it in calves' blood, and Strahl and Lieberkühn,* and recently Garrod,† maintain that they have detected it in human blood: without doubting the correctness of the observations of these chemists, it is only recently that I have been able to convince myself with precision by decisive experiments that urea is present in normal blood.

In my investigations regarding the amount of alkaline carbonates contained in the blood, I often operated on four or six pounds of fresh ox-blood: in order to avoid the decomposition and re-arrangement of the soluble mineral constituents of blood which always occur in ordinary incineration, I first separated the coagulable matters of the blood, after diluting it with four times its volume of water, and neutralising it with acetic acid; the residue left by the evaporation of the fluid, from which the coagulated albumen had been removed by filtration, and the films that formed during evaporation had been skimmed off, was treated with absolute alcohol, and then, in the manner we have already described, examined for urea; the measurements of the angles of the crystals both of nitrate and oxalate of urea, which were made according to Schmidt's method under the microscope, exactly coincided with the measurements given by Schmidt for these crystals.

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* Preuss. Vereins-Zeit. No. 47, 1847.

† Medico-Chirurgical Transactions. Vol. 31, p. 83.

Strahl's method, which I have repeatedly tried, and which consists in the extraction of the urea from four ounces of blood by the addition of alcohol, and in diagnosing the existence of urea from the crystallisation of the oxalate, does not appear to me to be sufficiently conclusive; for, in the first place, the quantity of urea in four ounces is very small, even for microscopic observation; secondly, alcohol extracts from the blood certain organic matters which partly separate on evaporation; thirdly, oxalic acid always precipitates mineral matters which render the object indistinct; and, finally, if its crystals be not crystallographically determined, it is often very hard to distinguish oxalate of urea from crystallised alkaline oxalates; all of which reasons led me to think that Strahl's experiments required to be confirmed in some other manner.

Urea increases abnormally in the blood of persons suffering from degeneration of the kidneys, whereby the function of those organs is destroyed. Under the general term of *Bright's disease*, we usually include the various conditions in which there is a mechanical disturbance of the urinary secretion, however different the histological alteration in the renal tissue may be; and we use the word *uræmia* to indicate the group of symptoms which depend on the retention of urea in the blood.

Christison[*] was the first who recognised the occurrence of urea in the blood in this disease. In any other disease, urea is only rarely found in the blood; hence, it is by no means requisite that the symptoms of uræmia should be combined with the presence of urea in the blood, since every physician knows how often Bright's disease occurs without this group of symptoms; it is only when the urine is very scanty that these symptoms occur: that of vomiting is not by any means a necessary one, as is generally supposed. Moreover urea has been found by Rainey[†] and Marchand, in the blood of cholera patients, but only when there was ischuria; and Garrod[‡] thinks that he has found it in the blood of a gouty patient.

Rees[§] and Wöhler[||] have detected urea in *Liquor Amnii*, which, they are convinced, contained none of the mother's urine. Mack[*] and Scherer[†] however, failed in detecting any urea in this fluid.

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[*] On granular degeneration of the kidneys, &c. Edinburgh, 1839, p. 20.

[†] Lond. Med. Gaz. Vol. 23, p. 518.

[‡] Op. cit.

[§] Lond. Med. Gaz. Vol. 23, p. 462.

[||] Ann. d. Ch. u. Pharm. Bd. 58, S. 98.

[Rees[‡] has frequently met with small quantities of urea in milk. —G. E. D.]

Millon[§] found urea in the *vitreous* and *aqueous humours* of the eye, and Wöhler[‖] confirms the fact.

Urea has very often been found in *dropsical exudations.*

I have never been able to discover urea in serous exudations, unless at the same time there was disease of the kidneys; previous statements may possibly only have reference to dropsical fluids depending on Bright's disease, and not to those accumulations of fluid which arise from enlargement of the liver.

In Bright's disease, urea is found in all the serous fluids; thus Schlossberger[¶] once found it in an aqueous effusion in the cerebral ventricles.

The *matters vomited* in uræmia not unfrequently contain urea. (Nysten[**] and others).

Wright[††] has found urea in the *saliva* of a patient with Bright's disease, and also in that of a dog poisoned with corrosive sublimate.

Urea has been found by O. B. Kühn in a *biliary concretion;* and Strahl and Lieberkühn have recently detected it in the *bile* after the extirpation of the kidneys.

Origin.—Physiologists were long undecided regarding the seat of the actual formation of urea. Since urea had not been discovered in normal blood, many believed that they must adhere to the old view, that the excreta are formed in the excreting organs from the constituents of the blood, and that urea is thus first produced in the kidneys. They accounted for the circumstance that urea is, in certain morbid conditions, sometimes found in the blood and other fluids, by assuming that it was then resorbed from the kidneys or the urinary bladder. To overthrow this opinion, Prevost and Dumas,[‡‡] and subsequently Gmelin, Tiedemann, and Mitscherlich,[*] extirpated the kidneys of animals, and then found no inconsiderable quantity of urea in the blood; indeed, Marchand[†] induced all the symptoms of uræmia in a dog by the mere ligature of the renal nerves, and was able to recognise the presence of urea with the greatest certainty, not only in the blood, but also in the vomited matters.

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[*] Arch. f. phys. u. pathol. Ch. u. Mikr. Bd. 2, S. 218-224.

[†] Zeitschr. f. wissenschaftl. Zoologie. Bd. 1, S. 88-92.

[‡] Guy's Hospital Reports. New series. Vol. 1, p. 328.

[§] Compt. rend. T. 26, p. 121.

[‖] Ann. d. Ch. u. Pharm. Bd. 66, S. 128.

[¶] Arch. f. phys. Heilk. Bd. 1, S. 43.

[**] Journ. de Chim. méd. 1837. p. 257.

[††] Lancet, 1844. Vol. 1, p. 150.

[‡‡] Ann. de Chim. et de Phys. T. 23, p. 90.

The investigations of Marchand have thrown much light upon this subject; this accurate observer could only recover 0·2 of a gramme of urea from 200 grammes of serum to which 1 gramme of urea had been added; he shows that, even if the urea were only separated from the blood at the end of each successive hour, it could not have accumulated in such quantity as to have been discoverable by the present mode of investigation. The following consideration will give us an idea of the small quantity of urea which, according to Marchand's hypothesis, at the most can accumulate in the blood in one hour. From the experiments of Ed. Weber, which I have in part confirmed, we may assume that there are in an adult man at most 6 or 7 kilogrammes [16 to 19 pounds] of circulating blood; now, if in 24 hours 30 grammes of urea are discharged, at most only 1·25 grammes could accumulate in one hour in the whole mass of the blood, so that only 0·021$\frac{0}{0}$ could be contained in it; this minute quantity can, however, as we have already shown, only be detected in operating on very large masses of blood, and by the aid of the microscope. Hence it is easy to understand why, during my experiments with an animal diet, while the urine was loaded with urea, none of this substance could be discovered in the blood.

If it be now established, that the urea is not primarily formed in the kidneys, the question still remains to be answered, whether it is produced in the circulating blood or in the individual living organs, (as for instance, the muscles,) and from what materials it is principally formed. In the present state of our knowledge, we may answer, that the urea is formed in the blood, and that it is produced from materials that have become effete, the detritus of tissues, as well as from unserviceable and superfluous nitrogenous substances in the blood. No animal tissue presents such vital activity, is so much used, and so rapidly worn out, as muscular tissue; it is in this tissue that the metamorphosis of matter proceeds most rapidly and abundantly, and yet, in the large quantities of muscular fluid on which Liebig worked, he could detect no trace of urea, although he found substances from which he could produce urea artificially. We must therefore assume that these substances, as creatine and probably inosic acid, are decomposed in the blood, by the action of the alkalies and of free oxygen, into urea and other matters to be excreted. Moreover, my experiments showing that the superfluous nitrogenous food which enters the blood, and the fact that caffeine, glycine, (Horsford) uric acid, and alloxantin, (Wöhler and Frerichs*) soon after they have been taken, perceptibly increase the amount of urea in the urine, support the view that urea is formed in the blood. It is impossible to suppose that this nitrogenous food is first converted into tissue, and subsequently into urea, &c., for we cannot think that a process occurs here, analogous to that exhibited by the percussion-apparatus of Physicists, where a certain number of parts, effecting a percussion, give rise to the repulsion of an equal number of parts. Hence the conversion of this matter can occur in no other place than in the circulating blood, and therefore it is here that the urea must be formed.

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[*] Pogg. Ann. Bd. 31, S. 303.

[†] Journ. f. pr. Ch. Bd. 11, S. 149.

That the urea is formed from nitrogenous matters could not be doubted, even if it did not contain nitrogen (and that in so large a quantity); for it is especially after the use of highly nitrogenous food that we find an augmentation of its quantity in the urine. If, however, we should further inquire—from what substances is it produced, and what tissues principally contribute to its formation? we could not, in the present state of our knowledge, give any satisfactory answers to these questions. All that we know is, that urea is a very general product of the decomposition of nitrogenous matters, both naturally within the animal body, and artificially in the laboratory of the chemist. We have already said enough to show that urea is so common a product of the decomposition of nitrogenous bodies, that we could hardly any longer enumerate it among true organic substances, if we tried to establish a distinction between organic and inorganic matter. Moreover, when we treat of uric acid we shall show that, in all probability, a great part of the urea separated by the kidneys from the blood is the product of the decomposition of that acid.

What is the importance of urea in the fluids of the eye, and whether it has any importance, are questions which, at present, cannot be answered.

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* Ann. d. Ch. u. Pharm. Bd. 65, S. 337-8.

XANTHINE.—$C_5H_2N_2O_2$.

Chemical Relations.

Properties.—This body, which has also been named *uric oxide* and *urous acid*, occurs, when freshly precipitated, as a white powder, which is neither crystalline nor gelatinous; when dried, it forms pale, yellowish, hard masses, which, on being rubbed, assume a waxy brightness: it is very slightly soluble in water, is insoluble in alcohol and ether, has no action on vegetable colours, and when heated, becomes decomposed without undergoing fusion, developing much hydrocyanic acid and a very peculiar odour, but yielding no urea. It dissolves with considerable facility in ammonia, but on evaporation it loses the greater part of the ammonia, and separates into a yellowish foliaceous mass. It dissolves freely in the caustic fixed alkalies, from which, however, carbonic acid will separate it; it dissolves also in nitric acid without the development of gas, and in sulphuric acid, to which it communicates a yellowish colour; it is all but insoluble in hydrochloric and oxalic acids. It does not combine in definite proportions with acids, alkalies, or salts.

Composition.—As, from the want of definite combinations, the atomic weight of this body cannot be ascertained, we can only give the empirical formula which expresses the simplest relation of the elements in xanthine. This substance was analysed many years ago by Liebig and Wöhler[*], and recently by Bodo Unger[†], with similar results:

Carbon	.... 5 atoms	39·47
Hydrogen	.... 2 „	2·63
Nitrogen	.... 2 „	36·84
Oxygen	.... 2 „	21·06
		100·00

This body has been regarded as uric acid ($C_5H_2N_2O_3$) in a lower state of oxidation; but till some of its compounds or products of decomposition are analysed, scarcely an hypothesis can be suggested regarding its theoretical constitution.

This body is only classified here with the animal bases, amongst which it cannot properly be reckoned, because, in its elementary composition it presents much similarity with them, and in a physiological point of view, it approximates to urea, guanine, and cystine.

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[*] Pogg. Ann. Bd. 41, S. 393.

[†] Ann. d. Ch. u. Pharm. Bd. 58, S. 18.

Preparation.—Urinary calculi, in which this body occurs, are dissolved in a solution of potash, and the xanthine is precipitated from the filtered fluid by carbonic acid.

Tests.—From the circumstances under which it occurs, this body can only be confounded with uric acid or cystine; under the microscope it may, however, be readily distinguished from them by its amorphous condition. It differs chemically from uric acid, firstly, in its ready solubility in ammonia, (hence it is not precipitated from its potash-solution, like uric acid, by hydrochlorate of ammonia;) secondly, in its being separated from its potash-solution by carbonic acid, as a precipitate, free from the alkali; thirdly, in its dissolving in nitric acid without effervescence, and on evaporation, leaving a (not red, but) yellow mass, which does not become red on the addition of ammonia. It differs from cystine, not only in its amorphism, but also in its insolubility in hydro chloric and oxalic acids.

Physiological Relations.

Occurrence.—This body was discovered in a urinary calculus by Marcet, who, from its behaviour with nitric acid, gave it the name of *xanthic oxide*. It has only been found once since, by Stromeyer, in a large calculus removed from a child; and it was from this source that both Liebig and Wöhler, and Unger, obtained the materials for their analyses. Jackson* thought that he had found it in a specimen of diabetic urine, but his experiments do not prove that he actually met with this substance. Although I have repeatedly sought for it, I have never been able to find xanthine in diabetic urine; indeed it has never been found in any specimen of urine.

Strahl and Lieberkühn† believe that they have discovered xanthine in human urine, but from the reactions which they describe, the substance in question appears to have been guanine.

[Dr. Davy‡ believes that the urinary secretion of scorpions and spiders consists for the most part of xanthine. The substance he has discovered is doubtless the same as that which Gorup-Besanez and F. Will have regarded as guanine. See p. 173.—G. E. D.]

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* Arch. d. Pharm. Bd. 11, S. 182.

† Harnsäure im Blut u. s. w. Berlin, 1848, S. 112 ff.

‡ Edin. New Phil. Journ. Vol. 40, p. 338, and vol. 44, p. 125.

Origin.—So little is known of this substance in reference either to its chemical nature, or its occurrence in the animal body, that we cannot offer any conjecture regarding its genesis.

Many attempts have been made to convert uric acid into xanthine, but they have all been unsuccessful.

HYPOXANTHINE.

[Since the publication of the first volume of Professor Lehmann's work, Scherer* has discovered the occurrence of a white, crystalline, pulverulent substance in the spleen, and in the heart of man and the ox. On analysis it yielded:

Carbon	44·257
Hydrogen	3·219
Nitrogen	40·820
Oxygen	11·704
	100·000

Its formula is $C_5H_2N_2O$. Hence it is xanthine *minus* 1 equivalent of oxygen. Scherer has given it the name of *hypoxanthine.*—G. E. D.]

GUANINE.=$C_{10}H_5N_5O_2$.

Chemical Relations.

Properties.—This body is a yellowish-white crystalline powder, devoid of odour or taste, which can bear a temperature of 220° without loss of weight, is insoluble in water, alcohol, and ether, has no action on vegetable colours, and dissolves freely in hydrochloric acid and caustic soda; it unites with acids, forming unstable salts; on mixing its sulphate with a very large quantity of water, there is a separation of the hydrate of guanine, which does not lose its combined water till it is raised to a temperature of 100°.

Composition.—This body was discovered by Bodo Unger:† it was at first mistaken for xanthine, but subsequently, by analysis of the free body and its salts, it was ascertained to be a distinct, weak base. According to the formula deduced from his analyses, it consists of:

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* Ann. de Ch. u. Pharm. Bd. 73, S. 328.

† Ann. d. Ch. u. Pharm. Bd. 51, S. 395 ff, and Bd. 58, S. 28-31; Pogg. Ann. Bd. 65, S. 222-239, and Ann. d. Ch. u. Pharm. Bd. 59, S. 58-73.

Carbon	10 atoms	39·73
Hydrogen	5 „	3·31
Nitrogen	5 „	46·36
Oxygen	2 „	10·60
		100·00

Its atomic weight=1887·5. The hydrate consists, according to Unger, of 2 atoms of water and 3 atoms of guanine. On account of its basic nature, Berzelius* regards it as ammonia with a nitrogenous adjunct$=H_3N.C_{10}H_2N_4O_2$.

Combinations.—Like caffeine and theobromine, and other weak bases, guanine readily unites in several proportions with acids, but, like the above-named substances, parts with them readily on the addition of large quantities of water, so that the pure base, mostly as a hydrate, is separated, while an acid salt remains in solution.

Hydrochlorate of guanine: the neutral salt, $3(C_{10}H_5N_5O_2.HCl)+7HO$, crystallises in bright yellow needles, loses all its water under 100°, and all its hydrochloric acid above that temperature: the acid salt, $C_{10}H_5N_5O_2+2HCl$, loses half its hydrochloric acid at a moderate temperature: with bichloride of platinum it forms a crystalline compound, $C_{10}H_5N_5O_2.HCl+PtCl_2+4HO$, which is as insoluble in cold water as the ammonio-chloride of platinum, but dissolves very freely in hot water. The following basic hydrochlorate has also been obtained: $2C_{10}H_5N_5O_2+HCl$.

Sulphate of guanine, $C_{10}H_5N_5O_2.HO.SO_3+2HO$, crystallises in yellow needles, often an inch in length.

Nitrate of guanine was obtained by Unger in several proportions:

$$3C_{10}H_5N_5O_2+3NO_5+12HO.$$
$$3C_{10}H_5N_5O_2+4NO_5+12HO.$$
$$3C_{10}H_5N_5O_2+5NO_5+16HO.$$
$$3C_{10}H_5N_5O_2+6NO_5+18HO.$$

The phosphate, oxalate, and tartrate of guanine may also be obtained.

Guanine-soda, $C_{10}H_5N_5O_2+2NaO+6HO$, is precipitated from the soda-solution on the addition of alcohol: it is a foliaceous crystalline mass, which attracts carbonic acid from the air, and effloresces. At 100° it loses all its water; on the addition of water one portion of the guanine separates, and another portion remains in solution with an excess of soda. Guanine also unites with certain salts, as, for instance, with nitrate of silver, forming crystalline compounds.

Products of its metamorphosis.—Guanic acid, $C_{10}H_3N_4O_7$, (termed

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* Jahresber. Bd. 27, S. 678.

hyperuric acid by Unger,) is obtained by digesting for 24 hours, at a temperature of 125°, 3 parts of guanine, 5 of chlorate of potash, 5 of water, and 30 of hydrochloric acid; it crystallises in short rhombic prisms with oblique terminal surfaces, is devoid of colour, odour, and taste, reddens moistened litmus, is slightly soluble in water and in acids, but dissolves freely in the caustic alkalies and their carbonates, and on dry distillation yields hydrated cyanic acid, together with water and carbon.

Preparation.—Guanine was obtained by Unger from guano, which he digests with diluted milk of lime till the fluid, when boiled, no longer appears brown, but assumes a faint greenish-yellow colour; it is then filtered and treated with hydrochloric acid; in the course of a few hours the guanine, with a little uric acid, separates; the sediment is then dissolved in hydrochloric acid, from which it is deposited in a crystalline form as a hydrochlorate; from this the guanine is finally separated by ammonia.

Tests.—Guanine is especially to be distinguished both from xanthine and from uric acid by its forming distinctly crystallisable salts with acids. Moreover, the difference of its behaviour with nitric acid is quite sufficient to prevent it from being mistaken for uric acid.

Physiological Relations.

Occurrence.—Unger has, as we have already mentioned, found guanine in guano (the excrements of certain sea fowls); it has recently also been found in the excrements of spiders by F. Will and Gorup-Besanez,* who think it very probable that this substance occurs in the green organ of the river craw-fish, and in the Bojanian organ in the fresh-water mussel.

If the constant occurrence of this substance in the urine, which Strahl and Lieberkühn† regarded as xanthine, (but which, from its solubility in hydrochloric acid, would rather seem to be guanine,) be confirmed by further investigations, we should have to classify guanine among the general products of excretion of the animal organism.

Origin.—From everything connected with the occurrence of guanine there can be no doubt that, like the nitrogenous compounds to which it is allied, it is a product of the metamorphosis of the nitrogenous matters of the animal body. Nothing is, however, known, on which we can even hazard a conjecture regarding the conditions under which it is formed.

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* Gelehrte Anz. d. k. bair. Ak. d. Wiss. 1848, S. 825-828, [and more fully in a memoir "on guanine as an essential constituent of certain secretions of the invertebrata," in Ann. d. Ch. u. Pharm. Bd. 69, S. 117.—G. E. D.]

† Op. cit.

ALLANTOINE.—$C_8H_5N_4O_5.HO$.

Chemical Relations.

Properties.—This body forms colourless, hard prisms, of the rhombohedric primitive form, which have a strong vitreous brilliance; it is devoid of smell and taste, dissolves in 160 parts of cold water, and more easily in hot water; it crystallises from its hot alcoholic solution, is insoluble in ether, is unaffected by exposure to the atmosphere, does not redden litmus, and chars, when heated, without fusing. It dissolves in solutions of the caustic alkalies and their carbonates, when these are warmed, but crystallises from them in an unchanged condition as they cool; it is decomposed by concentrated caustic alkalies, taking up water and resolving itself into oxalic acid and ammonia ($C_8H_5N_4O_5 + 7HO = 4H_3N + C_2O_3$); when boiled with concentrated sulphuric acid, it also takes up water, developing carbonic acid and carbonic oxide, and leaving sulphate of ammonia. On warming it with nitric acid (of 1·2 to 1·4 specific gravity,) it becomes decomposed into urea and allantoic acid, (3 atoms of allantoine, taking up 7 atoms of water, yield 2 atoms of urea and 2 atoms of allantoic acid, for $C_{24}H_{15}N_{12}O_5 + 7HO = C_4H_8N_4O_4 + C_{20}H_{14}N_8O_{18}$.)

Allantoine enters into combination with the oxides of lead and silver.

Composition.—Liebig and Wöhler* were the first who accurately determined the composition of crystallised allantoine, and they deduced the above formula from its silver-compound, according to which it consists of:

Carbon	8 atoms	30·38
Hydrogen	5 „	3·16
Nitrogen	4 „	35·44
Oxygen	5 „	25·32
Water	1 „	5·70
		100·00

The atomic weight of the hypothetical dry allantoine=1862.5.

This body cannot be reckoned amongst the organic bases, since it does not combine with any acid; but from the analogy of its composition, and the circumstance that we cannot find a more appropriate position for it than amongst the nitrogenous products of the metamorphosis of animal matters, we deemed it best to insert it in this place. No rational formula can be assigned for it; we may, however, remark, that it exactly contains the elements of 4 atoms of cyanogen and 5 atoms of water.

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* Pogg. Ann. Bd. 31, S. 561.

Combinations.—The *silver-compound*, $C_8H_5N_4O_5.AgO$, is obtained by mixing nitrate of silver with a boiling saturated solution of allantoine, and then adding ammonia as long as a precipitate continues to be produced: it forms a white powder which, when examined microscopically, is found to consist of clear, perfectly spherical particles.

The *lead-compound* is obtained on boiling an aqueous solution of allantoine with oxide of lead; it is crystallisable.

Products of its metamorphosis.—*Allantoic acid*, $C_{10}H_7N_4O_9$, which is obtained in the manner we have already described, occurs as a tough, amorphous, white mass, soluble in water, but insoluble in alcohol and ether, and forms soluble salts with the alkalies and earths. (Pelouze.*) Attention has been drawn to the fact that this acid contains exactly 3 atoms of water more than uric acid under the older formula, ($C_{10}H_4N_4O_6+3HO=C_{10}H_7N_4O_9$.)

Preparation.—On evaporating the allantoic fluid of the fœtus of a cow or the urine of a young calf to a thin syrup, without permitting it to boil, and then allowing it to stand for a few days, we obtain crystals of allantoine mixed with phosphate and urate of magnesia; by stirring it with cold water and decanting, most of the viscid matter, consisting of urate of magnesia, is removed, while the crystals of allantoine and phosphate of magnesia rapidly sink to the bottom; hot water extracts the allantoine, leaving the magnesian salt undissolved; the solution of allantoine is then decolorized with animal charcoal, and evaporated till it recrystallises.

Allantoine may also be obtained artificially from uric acid (see "Uric acid") by boiling it with peroxide of lead, the products of decomposition being oxalate of lead, urea, and allantoine; when the boiling fluid has been freed by filtration from oxalate of lead, and allowed to cool, the allantoine separates in crystals.

Tests.—This body can only be recognised with certainty by an accurate determination of its crystalline form, or by an elementary analysis either of itself or its silver-compound.

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* Ann. de Chim. et de Phys. 3 Sér. T. 6, p. 69.

Physiological Relations.

Occurrence.—Vauquelin and Buniva thought that they had found allantoine in the Liquor Amnii of a cow, but Lassaigne* proved that it is peculiar to the Liquor Allantoidis. It has recently been found by Wöhler† in considerable quantity, in the urine of young calves. It has as yet been found nowhere else in the animal organism.

According to Wöhler, the allantoine from calves' urine presents the peculiarity that it differs in the character of its crystals from that which is obtained from the allantoic fluid or from uric acid; the crystals grow together in bundles, and their terminal surfaces are no longer distinct, while pure allantoine appears in isolated well-formed prisms. This difference, however, only depends on the admixture of a foreign substance, whose quantity is much too minute to produce any appreciable influence on the result of its elementary analysis. By combining it with oxide of silver, and then decomposing the compound, we obtain it in as pure and isolated a state as when we prepare it from the allantoic fluid or from uric acid.

Origin.—That allantoine is a product of the metamorphosis of nitrogenous food or of tissue in the animal organism, is sufficiently obvious from the circumstances under which it occurs, but any nearer indication of the chemical process on which its formation depends is impossible, since we have no idea of its rational composition. The two following facts may, however, probably indicate the way in which its formation may at some future time be explained: firstly, it only occurs in the urine of the fœtus and of recently-born animals, and disappears after the use of vegetable food; secondly, as has been discovered by Wöhler, it occurs in the urine of sucking calves, together with uric acid and urea, but without hippuric acid; hence the idea suggests itself that allantoine and hippuric acid exclude or stand in the place of one another, which might rather have been expected of uric acid, from which allantoine may be artificially prepared.

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* Ann. de Ch. et de Phys. T. 17, p. 301.

† Nachrichten der k. Gesellsch. d. Wiss. zu Göttingen, 1849. No. 5, S. 61-64; [and more fully in Ann. d. Ch. u. Pharm. Bd. 70, S. 229.—G. E. D.]

Cystine.—$C_6H_6NS_2O_4$.

Chemical Relations.

Properties.—This body occurs in colourless, transparent, hexagonal plates or prisms, is devoid of taste and smell, and is insoluble in water and alcohol; it dissolves in oxalic acid and in the mineral acids, forming with them saline combinations, most of which are crystallisable, but it does not unite with acetic, tartaric, or citric acid: it is decomposed by nitric acid, leaving, on the evaporation of the fluid, a reddish brown mass; it dissolves freely in the caustic fixed alkalies and their carbonates. It dissolves in caustic ammonia, but does not unite with it, so that on evaporation it crystallises unchanged. It is insoluble in carbonate of ammonia; hence it is best precipitated from its acid solutions by carbonate of ammonia, and from its alkaline solutions by acetic acid.

Cystine does not fuse on the application of heat, but it burns with a bluish green flame, developing at the same time a very peculiar acid odour; on dry distillation it developes a stinking empyreuma and ammonia, and leaves a voluminous porous coal. On boiling it with alkalies, ammonia is first developed, and subsequently an easily inflammable gas, which burns with a blue flame.

Composition.—Cystine has been analysed by Prout, Baudrimont, Thaulow,* and Marchand,† with perfectly identical results, yielding the above formula, according to which this substance contains:

Carbon	6 atoms	30·000
Hydrogen	6 „	5·000
Nitrogen	1 „	11·666
Sulphur	2 „	26·667
Oxygen	4 „	26·667
		100·000

Its atomic weight=1336·0.

Since cystine, which has also received the name of *cystic oxide*, unites with certain acids to form crystalline salts, Berzelius classifies this body with the combinations of conjugated ammonia $=H_3N.C_6H_3S_2O_4$. If, however, this view be correct, much is still wanting for the establishment of the rational formula of cystine, for the most important question regarding its constitution still remains unexplained, namely, in which form or combination the sulphur is contained, in the cystine or in this adjunct. The chemical investigations regarding cystine, which have been hitherto instituted, do not tend to support any hypothesis.

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* Ann. d. Ch. u. Pharm. Bd. 27, S. 197.

† Journ. f. pr. Ch. Bd. 10, S. 15-18.

Combinations.—Hydrochlorate of cystine, $C_6H_6NS_2O_4.HCl$, crystallises without water in plates grouped in a star-like form. Berzelius* obtained the combination with bichloride of platinum by direct union; this salt is not crystallisable; it dissolves easily in water and alcohol, but is insoluble in ether.

Nitrate of cystine, $C_6H_6NS_2O_4.HO.NO_5+HO$, crystallises readily, losing its one atom of water at 85°.

Preparation.—Urinary calculi, in which cystine occurs, are dissolved in a solution of potash, and the cystine is precipitated from this solution by acetic acid; or we dissolve them in ammonia, and allow the filtered fluid to evaporate in the air.

Tests.—Cystine is characterised by the readiness with which it crystallises in well-formed hexagonal plates, which may be distinguished with great ease under the microscope, and by its solubility both in alkalies and mineral acids. Further, it may be known by the peculiar odour which it developes on dry distillation and on burning, which is unlike that evolved by any other similar substance. Liebig has given the following test for cystine. The potash-extract of the substance in which we are searching for cystine must be decomposed with a solution of oxide of lead in caustic potash; if, on the application of heat, there be a precipitation of sulphide of lead, cystine is probably present; we must, however, previously satisfy ourselves that no other sulphurous body, as, for instance, mucus, albumen, &c. be simultaneously present.

If cystine be mixed with a small quantity of the urates, the two substances may be separated by the aid of boiling water, in which the former is insoluble. Uric acid occasionally appears under the microscope in the form of hexagonal tablets, but we should never trust in these cases to microscopic examination alone.

Physiological Relations.

Occurrence.—Cystine was originally discovered by Wollaston,† in a urinary calculus. Calculi of this nature, although very rare, have since been found by many other chemists, as, for instance, Prout, Taylor, Baudrimont, Lassaigne, Dranty, Civiale, Buchner, and Bird. Bird* and Mandl† remark that they have often found cystine dissolved in the urine, from which Bird precipitates it by acetic acid; it also occurs as a sediment mixed with urate of soda. The pathological process accompanying the appearance of cystine in the urine is altogether unknown. Bird thinks there is some connexion between it and the scrofulous diathesis; others fancy that they see a connexion between cystine and diabetes; but none of these conjectures are supported by the results of experience. In the examination of 129 urinary calculi, Taylor found only two that contained cystine. This substance has been found nowhere but in the urine.

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* Jahresber. Bd. 27, S. 631.

† Phil. Trans., 1810, p. 223.

Origin.—As no other urinary constituent contains sulphur‡, the occurrence of this highly sulphurous body in the urine is the more singular, and we should consequently expect that some essential alteration of the chemico-vital processes must have taken place before this substance could be produced, but all that we learn from the simultaneous morbid phenomena completely disappoints us in the assumption that the excretion of cystine must probably be preceded by a certain group of symptoms, from which something might be concluded regarding the production of this body. Taurine is the only other body with which we are acquainted that is equally rich in sulphur; no other animal bodies in which sulphur occurs, as albumen, casein, fibrin, &c. contain at most more than $2\frac{0}{0}$, while in this substance there is $25\frac{0}{0}$. Hence, in a chemical point of view, a connexion might be suspected between taurine and cystine, and the rational physician should consequently direct his attention to the manner in which the functions of the liver are performed, whenever cystine presents itself in the urine.

Taurine.—$C_4H_7NS_2O_6$.

Properties.—This substance which was formerly termed *biliary asparagin*, crystallises in colourless, regular hexagonal prisms with four and six-sided sharp extremities, (the elementary form is that of a right rhombic prism, the angles formed by the edges of the sides being 111°44 and 68°16); it is hard, craunches between the teeth, has a cooling taste, resists the action of the atmosphere, dissolves in 15·5 parts of water, and in 573 of spirit of wine (of 0·835 specific gravity,) but is insoluble in anhydrous alcohol and ether, and has no action on vegetable colours. It dissolves, without undergoing change, even at the boiling point, in the mineral acids, but forms no compounds with them. It is not precipitated from its solution either by tannic acid or by the metallic salts. On heating, it fuses, puffs up, and developes much acetate of ammonia, and a thick brown oil; if it be inflamed in the air, it developes much sulphurous acid; if it be dissolved in caustic potash, and the solution boiled down till it becomes thick, it developes pure ammonia gas, and leaves a residue consisting solely of sulphite and acetate of potash. The sulphur in taurine cannot be detected in the moist way either by nitric acid or by aqua regia.

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* Urinary Deposits, &c. 3rd Edition, p. 188.

† Journ de Chim. méd. 1838, p. 355.

‡ [This statement is too general. Dr. Ronalds has shewn that the extractive matters of the urine contain an unknown sulphur-compound. See Phil. Trans. 1846, p. 461. G. E. D.]

Composition.—Taurine was first discovered by Gmelin in the bile, and was soon afterwards analysed with very similar results by Demarçay, Pelouze, and Dumas; these chemists, however, entirely overlooked the existence of sulphur in this body, the discovery of which was reserved for Redtenbacher,* from whose analyses it was found to consist of:

Carbon	4 atoms	19·20
Hydrogen	7 „	5·60
Nitrogen	1 „	11·20
Sulphur	2 „	25·60
Oxygen	6 „	38·40
		100·00

As this body has not yet been combined with any other in a definite proportion, its atomic weight cannot be determined with accuracy; but it must not be reckoned among the bases, and we are still perfectly in the dark regarding its rational composition. Redtenbacher† attempted to elucidate this point; finding that by the action of potash taurine was decomposed into ammonia, acetic acid, and sulphurous acid, he was somewhat inclined to believe that taurine is a combination of sulphurous acid with aldehyde and ammonia (since $2SO_2 + H_3N + C_4H_4O_2 = C_4H_7NS_2O_6$), and that it might probably be artificially prepared from these substances, as urea is obtained from cyanate of ammonia. Indeed, on passing sulphurous acid into an alcoholic solution of aldehyde-ammonia he obtained a white crystalline body isomeric with taurine; it is however not identical with taurine, but must be regarded as an acid sulphite of aldehyde-ammonia; it reddens litmus, gradually changes on exposure to the air, turns yellow at 100°, and at a higher temperature becomes brown, and finally developes an odour resembling that of burned taurine. Hence, notwithstanding these ingenious experiments of Redtenbacher's, the rational constitution of taurine remains still unexplained.

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* Ann. d. Ch. u. Pharm. Bd. 57, S. 170-174.

† Ibid. Bd. 65, S. 37-45.

Preparation.—Taurine is usually obtained from ox-gall. The bile, freed from its mucus by an acid, or its alcoholic extract, is mixed with hydrochloric acid, and boiled for some hours till the choloidic acid is completely formed from the nitrogenous acids of the bile; the acid fluid, after the removal of the choloidic acid by filtration is rapidly evaporated, causing the chloride of sodium to crystallise; the acid mother-liquid is then treated with five or six times its bulk of boiling alcohol, from which, as it cools, the taurine separates in needles; by recrystallisation in water it is obtained in a state of purity.

Tests.—Taurine may be distinguished from every other substance by its crystalline form (which under the microscope is as distinct in small crystals as in large ones), by its property of developing sulphurous acid when heated in a glass tube open at both ends, or on a platinum spatula, and finally, by the circumstance that when boiled with caustic potash, it does not form a black solution, but developes ammonia, and leaves a residue consisting solely of sulphurous and acetic acids in combination with potash.

Physiological Relations.

Occurrence.—Taurine has never been found isolated in the healthy organism; it appears to be contained preformed in normal bile, and to occur there as an adjunct of the already described cholic acid; at all events it only occurs in an isolated state in decomposed or morbid bile. After the removal of the mucus, the only sulphur-compound, in those animals in which the bile contains sulphur, is taurine conjugated with cholic acid. At the present time we know, by the researches of Bensch,* that sulphur exists in the bile of the ox, the sheep, the fox, the bear, the dog, the wolf, the goat, the domestic hen, and certain fresh-water fish; and Schlieper† has found it most abundant in the bile of serpents. From the bile of the pig Strecker and Gundelach‡ were unable to obtain taurine, and they found no sulphur in it, although Bensch had detected a small quantity. Doubts have been expressed whether sulphur, and consequently taurocholic acid, exists in human bile, but Gorup-Besanez* has so completely set this point at rest, that my evidence founded on the crystallometric determination of taurine artificially obtained from human bile is superfluous. In diseased bile taken from the dead body taurine is especially found when, as is sometimes the case, the bile has an acid reaction; thus Gorup-Besanez found taurine in the bile of a person who had died from arachnitis.

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* Ann. d. Ch. u. Pharm. Bd. 65, S. 194-203.

† Ibid. Bd. 60, S. 109-112.

‡ Ibid. Bd. 62, S. 205-232.

Although some of the products of the decomposition of bile occur in the excrements, especially in cases of diarrhœa, taurine has never yet been found there: neither has it been detected in bilious urine.

Origin.—If we consider that the excreted products of the animal organism are usually highly oxidised organic matters, and that most of the matters separated from the blood and even deposited in the tissues, differ from the food in containing a larger amount of oxygen, it must at first sight strike us as singular that a substance so rich in sulphur as taurine either alone or in combination, should be produced, even in the normal state of the body, from the animal fluids, which are almost universally saturated with free oxygen. Although Redtenbacher failed in obtaining taurine artificially, his admirable researches render it highly probable that the sulphur in taurine exists in an oxidised state, as indeed may be inferred from the fact that it cannot be recognised in this substance by means of the ordinary fluid oxidising agents. The genesis of taurine should therefore not be sought in a de-oxidising process in the blood, (a very improbable process,) but rather in a process of oxidation. If, however, taurine be the product of an oxidation, the source of its formation should hardly be sought in the liver, since the blood that is poorest in oxygen is supplied to this organ. This simple induction leads us to refer the seat of the formation of taurine, or at least of its proximate constituents, to the blood, where, however, it cannot be detected for the same reason that so long prevented the presence of urea from being ascertained. Nothing is at present known regarding the different steps that occur in the formation of taurine; it is, however, not improbable that the sulphur of the albuminous food in its conversion into the elements of tissues, which are either free from or poor in sulphur, yields in part the materials for the formation of taurine.

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* Unters. üb. Galle. Erlangen, 1846. S. 31-37.

Uses.—If we can conjecture with some probability regarding the origin of taurine, we are even less fortunate in reference to the function which the taurine excreted with the bile in the intestine, exerts in the animal organism, since in this point of view we are entirely devoid of facts on which to hang even a bare induction. No conclusion can be drawn regarding the further use of this substance in the animal body, from the negative fact that hitherto no taurine has been found in normal excrements, since accurate and sufficiently minute experiments have not yet been made on this subject. As there are some animals, as, for instance, the pig, which, although they secrete bile copiously, separate no taurine by the hepatic organs, it appears that at all events it is unimportant to the process of digestion. But that taurine, even if first separated from the blood, should be again resorbed from the intestine into the blood, and being there burned, should serve as a material for supporting the animal heat, appears to us not impossible, but certainly improbable. (See "Taurocholic Acid.")

CONJUGATED ACIDS.

Although we may not feel justified in directly introducing into physiological chemistry all the transient views which have arisen in theoretical chemistry; and although we would wish to abstain from those more than hypothetical opinions regarding the theoretical constitution of organic bodies, which are for ever rising, and as rapidly disappearing; yet we ought not to omit all reference to the present state of theoretical chemistry, but should be ready to appropriate to physiological chemistry every acquisition which seems likely to be fruitful in results. It would by no means further the progress of physiological chemistry at once to transfer to it all the hypotheses or fictions that may have been advanced in pure chemistry. If we were to attempt to support these chemical hypotheses with others of a physiological nature, the foundation of physiological chemistry would be very unstable, and finally the whole superstructure would be an aerial image of the fancy (and of these images we have already an abundance) rather than an experimental science based on pure induction. It is, however, necessary for the progress of science, that in accordance with the present state of chemical theory we should establish certain general propositions, which not only furnish us with a comprehensive expression for a number of frequently recurring facts, but guide inquiry in various directions, and finally present us with certain points of support for the due understanding of our scientific material. Amongst these general propositions we reckon the method which is now becoming tolerably common in theoretical chemistry, of considering certain bodies as conjugated or copulated combinations. We shall, however, place no more exclusive dependence on this theory, as it has been carried out by Laurent and Gerhardt,[*] or Strecker,[†] or Kolbe,[‡] than on the theory of organic radicals and of electro-chemical dualism of a Berzelius, or on the theory of substitutions and metalepsy of a Dumas. If we even venture on a reference to eclecticism, it must be in the choice of those supports which one branch of science, in its early stage, is compelled to borrow from another. It is only in this point of view that we wish to justify the establishment of the group of conjugated acids in zoo-chemistry.

We have already had occasion to refer to a series of organic acids which, according to the excellent investigations of Kolbe, may be regarded as carbo-hydrogens conjugated with oxalic acid: indeed, Kolbe is inclined to regard all the groups of acids we have noticed, which contain 3 atoms of oxygen, as combinations of oxalic acid with carbo-hydrogens. These illustrations are sufficient to indicate the idea which we attach to the expression, *conjugated* or *copulated acids*. We have become acquainted with acids which, in opposition to the ordinary rules of chemistry, not only lose nothing of their acidity, but (which is most singular) perfectly retain their former saturating capacity, when united with another and a more basic body; after being combined with the so-called adjunct (copula), this acid still saturates the same quantity of base as if the organic matter associated with it did not exist; and this dependent—the adjunct—which follows the acid as an integral constituent in all its combinations, exerts an essential influence on its physical and even on many of its chemical properties. Thus, for instance, oxalic acid, which in its ordinary state is so readily decomposed by heat, becomes volatile by its conjuga-

[*] Ann. de Chim. et de Phys. 3 Sér., T. 24, p. 200-208.

[†] Ann. d. Ch. u. Pharm. Bd. 68, S. 47-55.

[‡] Handwörterb. d. Chemie. Bd. 3, S. 439-444.

tion (accouplement) with the above-named carbo-hydrogens; the stability is, however, most obvious in those acids in which such easily decomposable bodies as hyposulphurous or hyponitric acid are conjugated; their salts being altogether dissimilar from those of the non-conjugated acids in their crystalline form, solubility, amount of water, &c.

In combinations of this kind the electro-chemical polarity is entirely lost; the older dualistic views of chemistry here altogether fail us; we must therefore here assume another ground of chemical attraction than that of opposite polarity, and this view is confirmed by the circumstance that these compounds cannot be decomposed according to our ordinary chemical principles, that is to say, by simple or double elective affinity. They also no more admit of being decomposed into their proximate constituents, that is to say, into the acid and the adjunct, than of being directly formed from them. Most of the conjugated acids are only formed when the adjunct in its nascent state comes in contact with the acid; and conversely it is only very few of them that can be decomposed into the acid and the adjunct, and even in this case the adjunct invariably assimilates water, and it is impossible to determine with certainty whether the isolated hydrated body in its anhydrous condition actually constituted the adjunct, or whether the latter body was represented by some other group of atoms. This favourable condition, however, very rarely aids us; for generally, in our attempts to separate the adjunct from the acid, the former becomes so decomposed that we can arrive at no conclusion regarding its nature: and this is the reason why chemists, when they enter into the general consideration of the laws of conjugated acids have to trust more or less to hypotheses; and it would scarcely be in accordance with our views to follow their track. We shall, however, be compelled to devote some attention to these hypotheses when we treat of the acids of this class, pertaining to zoo-chemistry; and we will here only remark that we will subsequently treat of those combinations of organic acids with organic oxides in which all acidity has disappeared, and which have been named by Berzelius *haloid salts*, whilst other chemists of the present day have included them in the category of conjugated compounds.

Most of the known conjugated acids are formed by the action of sulphuric or nitric acid on organic substances. In the following group, picric acid is the only one we will consider in any detail, partly by way of general illustration, and partly because it occurs more frequently than the others as a product of the decomposition of different nitrogenous substances by nitric acid. The other acids of this class, to which reference may be made in zoo-chemistry, will be considered under the head of the substances from which they are derived.

There are but few of the pure organic acids whose adjunct can be determined with much probability. It necessarily arises from the nature of these substances, that conjugated organic acids can be decomposed into acids and their adjuncts with much less facility than the conjugated mineral acids, and that their proximate constituents cannot be ascertained without difficulty. We have ventured in the following pages to enumerate nitrogenous organic acids in the group of conjugated acids, not that the composition of each one can with certainty be referred to a nitrogenous adjunct and an acid, but because the study of the products of decomposition of such bodies renders it tolerably evident that all nitrogenous acids, more especially on account of their high atomic weight, are composed of proximate constituents, of which the nitrogenous one scarcely at all contributes to the acidity of the combination.

This, however, is pure conjecture; but, at the same time, in considering the nitrogenous acids, we should have to adopt an arbitrary classification, if we were to consider those in which the conjugate constitution has to any extent been proved, distinct from those in which no evidence of this nature has been obtained. Between these two classes there exist so many analogies that it would be of no practical utility to attempt such a separation.

Picric Acid.—$C_{12}H_2N_3O_{13}.HO$.

Properties.—This acid, which was formerly known as *carbonitric acid*, *carbazotic acid*, and *Welter's bitter*, crystallises in yellow, glistening plates or prisms, fuses when carefully heated, and admits of being sublimed undecomposed, but when rapidly heated decomposes with explosions; it is devoid of odour, has a very bitter taste, and dissolves slightly in cold and readily in hot water, the solution being of a yellow colour; it dissolves freely in alcohol and ether, and reddens litmus; when heated with phosphorus or potassium it decrepitates violently; it is not decomposed by chlorine, nitric or hydrochloric acids, or by *aqua regia*.

Composition.—According to the above formula this acid consists of:

Carbon	12 atoms	31·44
Hydrogen	2 „	0·87
Nitrogen	3 „	18·34
Oxygen	13 „	45·42
Water	1 „	3·93
		100·00

The atomic weight of the hypothetical anhydrous acid = 2750·0; and its saturating capacity = 3·636. Chemists are not agreed regarding the rational formula of this body; they unite in regarding it as a conjugated nitric acid, but there is much difference of opinion regarding the nature of the adjunct. Berzelius writes this acid as $=(C_{12}H_2NO_3.NO_5)+NO_5.HO$, but there is little to support the view of a salt-like adjunct such as is here assumed. We know, for instance, that the group of atoms NO_4 is substituted in aniline and certain other bodies for an equivalent of hydrogen, and it is now pretty generally assumed that such substitutions of more negative matters in the place of hydrogen for the most part only extend to the hydrogen contained in the adjunct; if, therefore, we assign to picric acid only a hypothetical formula, it will at all events not be an irrational one, if we consider that in the adjunct $C_{12}H_4$, 2 atoms of hydrogen are replaced by 2 atoms of NO_4, and write the acid as $=C_{12}(H_2.2NO_4).NO_5.HO$. Laurent regards picric acid, not as a conjugated acid, but as carbolic acid $(C_{12}H_5O)$ in which 3 atoms of hydrogen are replaced by 3 atoms of NO_4, and hence he writes it as $=C_{12}(H_2.3NO_4)O.HO$.

Combinations.—The *picrates* are crystallisable, yellow, and for the most part soluble in water; when rapidly heated they decrepitate with much violence.

Picrate of potash is one of the most insoluble salts of this acid; it crystallises in long, glistening, yellow, iridescent prisms, and dissolves in 260 parts of cold, and 14 parts of hot water. With alkaline earths and metallic oxides this acid has a tendency to form basic and very insoluble salts.

Preparation.—This acid is formed by the action of concentrated nitric acid on many vegetable and animal substances. Thus, for instance, in heating salicin with nitric acid, we obtain crystals of pure picric acid. It is likewise produced in large quantity on decomposing silk with nitric acid; it is, however, most commonly obtained by boiling indigo with nitric acid.

HIPPURIC ACID.—$C_{18}H_8NO_5.HO$.

Chemical Relations.

Properties.—Hippuric acid, known also as *uro-benzoic acid*, separates from hot solutions on cooling, in the form of minute spangles, or of larger, obliquely-striated, four-sided prisms, terminating at the ends in two flat surfaces. The elementary form of the crystals is a vertical rhombic prism, which is best studied in microscopical crystals obtained by the slow evaporation of a solution of hippuric acid, which are similar to those of phosphate of ammonia and magnesia, even in their most varied combinations. (C. Schmidt.*) This acid is devoid of smell, has a slightly bitter but not an acid taste, dissolves in 400 parts of cold water, and very freely in hot water; it is moreover readily soluble in alcohol, but difficult of solution in ether. Even the cold aqueous solution reddens litmus powerfully.

When gently heated, hippuric acid fuses, without loss of water, into an oily liquid, which, on cooling, solidifies into a crystalline milk-white mass; on the application of a stronger heat, there is produced a crystalline sublimate of benzoic acid and benzoate of ammonia, while a few oily drops are at the same time formed, which evolve an odour of cumarin (the oil of the Tonka bean,) or fresh hay, solidify on cooling, and are soluble in alcohol and ammonia, but not in water. On exposing the acid to a more rapid and stronger heat, an intense odour of hydrocyanic acid is developed, and a porous coal is left as a residue.

Hippuric acid is unaffected by chlorine, chlorous, and dilute mineral acids; but when heated with concentrated hydrochloric or nitric acid, or even with oxalic acid, it becomes decomposed (as already mentioned in page 152,) into benzoic acid and glycine (Dessaigne†). When heated with peroxide of manganese and sulphuric acid it is decomposed into carbonic acid, ammonia, and benzoic acid (Pelouze); boiled with freshly prepared peroxide of lead it yields benzamide, carbonic acid, and water (Fehling); and finally, if it be dissolved in nitric acid, and a stream of nitric oxide gas be passed through the solution, there is a development of ammonia, whilst there remains in solution a new non-nitrogenous acid which $=C_{18}H_7O_7.HO$. (Strecker.)

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* Entwurf u. s. w. S. 36—40.

† Compt. rend. T. 21, pp. 1224-1227.

Heated with hydrate of lime or caustic potash, hippuric acid yields benzine and ammonia, while the residue consists solely of carbonate of [lime or] potash, without a trace of cyanide of [calcium or] potassium. In fermenting and putrefying fluids this acid becomes decomposed into benzoic acid and other yet unknown products.

Shortly after Liebig's discovery of hippuric acid, while preparing it in large quantities from the urine of horses, I obtained one isolated crystal of hippuric acid half an inch in length, in which the vertical rhombic prism of the elementary form ∞ P was combined with 2 microdiagonal horizontal prisms, whereby the combining corners were truncated by the brachydiagonal horizontal prism. I have never again succeeded in obtaining crystals of such size and thickness.

Composition.—According to the above formula hippuric acid consists of:

Carbon	18 atoms	60·335
Hydrogen	8 ,,	4·469
Nitrogen	1 ,,	7·821
Oxygen	5 ,,	22·347
Water	1 ,,	5·028
		100·000

The atomic weight of the hypothetical anhydrous acid=2125·0; and its saturating capacity=4·706.

From the various modes in which hippuric acid may be disintegrated, corresponding views have been taken of its constitution; all, however, agree in the opinion that in hippuric acid there must be concealed the radical *benzoyl*, $C_{14}H_5$, which is common to benzoic acid, volatile oil of bitter almonds, and benzamide. From the behaviour of hippuric acid with peroxide of manganese and sulphuric acid, and from the composition of formobenzoic acid, which, as may be shown, consists of formic acid and oil of bitter almonds, (hydride of benzoyl,) Pelouze* concluded that hippuric acid was a kind of formobenzoic acid, which had assimilated hydrocyanic acid, so that it consisted of 1 equivalent of hydrocyanic acid, 1 equivalent of hydride of benzoyl, and 1 equivalent of formic acid, and $=H.C_2N+H.C_{14}H_5+C_2HO_3.HO$.

This view of the composition of hippuric acid also finds some support in the circumstance that amygdalic acid, according to the recent investigations of Wöhler,† seems most probably to be formic acid, with oil of bitter almonds and sugar as an adjunct. If hippuric acid were actually composed in this manner, the products of decomposition with peroxide of manganese, could be hardly different from what they are, for hydrocyanic acid is very readily decomposed into formic acid and ammonia, and the oxygen yielded by the manganese converts the formic into carbonic acid, and the hydride of benzoyl into benzoic acid—both being processes of very frequent occurrence. But independently of the circumstance that, at least in analogous processes, some formic acid remains undecomposed, this view is also opposed by the fact that other oxidising agents do not decompose hippuric acid in the same manner which they undoubtedly would do if the acid actually had this composition. On this account Fehling,* influenced by the behaviour of hippuric acid with peroxide of lead, regarded it as fumaric acid conjugated with benzamide, and $= H_2N.C_{14}H_5O_2 + C_4HO_3.HO$. If benzoic acid existed preformed in hippuric acid, it would be very unlikely that, by the action of an oxidising agent, as peroxide of lead, a substance so poor in oxygen as benzamide should be formed.

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* Ann. de Chim. et de Pharm. T. 26, pp. 60-68.

† Ann. d. Ch. u. Pharm. Bd. 66, S. 238-242.

Dessaigne's remarkable discovery must lead to the conclusion that glycine exists preformed in hippuric acid, and is conjugated with benzoic acid, so that 1 atom of anhydrous glycine with 1 atom of benzoic acid forms hydrated hippuric acid, since $C_4H_4NO_3 + C_{14}H_5O_3 = C_{18}H_8NO_5.HO$; but if we are not altogether opposed to Strecker's formula for the formation of conjugated compounds from their constituents with the loss of certain atoms of water, yet it appears to us simple and natural that we should only compare with one another the formulæ of anhydrous combinations, and that certain atoms of water should not be arbitrarily abstracted; anhydrous glycine and anhydrous benzoic acid yield 1 atom of hydrogen and 1 atom of oxygen more than anhydrous hippuric acid contains: if now, notwithstanding this, we assume that glycine exists preformed in hippuric acid, with however only a small quantity of water, we should proceed just as irrationally as if we assumed that ammonia existed in oxamide or in benzonitrile, because these bodies, when they assimilate water, yield ammonia. All, therefore, that we can maintain is, that in hippuric acid we find, in addition to benzoic acid, an adjunct $= C_4H_3NO_2$, which, on its separation, has a strong tendency to be transformed into glycine—a substance which is as readily formed as urea in the decomposition of nitrogenous matters, (see pp. 152 and 158.) It is in the changes which the adjunct undergoes in its intimate constitution by the action of stronger agents, that we must seek to ascertain the reason why the fixed acid is freed from the adjunct. This adjunct of hippuric acid might be regarded, in reference to its composition, as an amide of fumaric acid ($C_4H_3NO_2 = H_2N.C_4HO_2$), and we should thus arrive at the reverse of Fehling's view of the subject. The question therefore now remains—Is it more probable that in hippuric acid benzamide is combined with fumaric acid, or fumaramide with benzoic acid? or is it more probable that in the action of peroxide of lead the benzoic acid is converted into benzamide by the oxidation of the fumaramide, or that by the action of concentrated acids the benzamide is decomposed and fumaramide formed? No satisfactory answer to these questions can be deduced either from the laws of stoichiometry or of affinity; since most unquestionable observations show in both cases the remarkable fact of the alternating substitution of 1 atom of amide and 1 atom of oxygen, (for in the conversion of benzoic acid into benzamide the former takes in exchange 1 equivalent of amide for 1 atom of oxygen, and a similar substitution occurs in the conversion of fumaric acid into fumaramide.) If, however, we regard benzoic acid as existing preformed in hippuric acid, we are by no means constrained to assume that the adjunct is fumaramide, or indeed any amide-compound. If we represent the formula of hippuric acid $= C_4H_3NO_2.C_{14}H_5O_3.HO$, this view is supported in the first place by the circumstance that hippuric acid has many physical and chemical properties in common with benzoic acid, which lead to the assumption that benzoic acid exists preformed in it, but afford no presumption in favour of the pre-existence of benzamide or fumaric acid in it. Secondly, we are indebted to the labours of Strecker for our knowledge of another conjugated acid, in whose analogous decomposition by acids glycine is also separated, which here also can only be produced by the assimilation of water; this acid being the biliary acid presently to be considered, where the same adjunct is combined with the cholic acid which we have already described. Thirdly, the fact discovered by Wöhler that benzoic acid, in its passage through the animal organism, is converted into hippuric acid, affords a certain amount of support to this view.

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* Ann. d. Ch. u. Pharm. Bd. 28, S. 48.

Recently, however, Strecker* has been led to yet another view regarding the constitution of hippuric acid from its behaviour with nitric oxide, and from the formation of the acid whose formula $= C_{18}H_7O_7.HO$. He looks upon hippuric acid as an amide-compound of this acid, and $= H_2N.C_{18}H_7O_7$; but the amides never have acid properties (besides which this only represents the hydrated hippuric acid); if Strecker had not ascertained that the silver-salt was accurately represented by $AgO.C_{18}H_7O_7$, we might have regarded its composition as expressed by the formula $C_9H_3O_3.HO$, and therefore have considered hippuric acid as analogous to oxamic, lactamic, tartramic, and aspartic acids, and as a compound of this acid with its amide ($H_2N.C_9H_3O_2 + C_9H_3O_3.HO = C_{18}H_8NO_5.HO$). The view, in accordance with which benzoic acid exists preformed, is, however, still the most probable.

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* *Ann. d. Ch. u.* Pharm. Bd. 68, S. 53.

Combinations.—With alkalies and alkaline earths hippuric acid forms crystallisable salts soluble in water and having a bitter taste; its combinations with metallic oxides are difficult of solution in cold water, but dissolve somewhat more freely in hot water. All the crystallised salts contain water of crystallisation. Schwartz* has analysed the following salts:

Neutral hippurate of potash, $KO.\overline{Hi} + 2HO$, occurs in microscopic, oblique rhombic prisms, which part with their water at 100°. The acid salt $KO.\overline{Hi} + HO.\overline{Hi} + 2HO$, crystallises in broad, satiny plates.

Hippurate of soda, $2NaO.\overline{Hi} + HO$, is crystalline, and dissolves readily in water and alcohol.

Acid hippurate of ammonia, $H_4NO.\overline{Hi} + HO.\overline{Hi} + 2HO$, occurs in very minute, four-sided, square prisms; it behaves, when thrown upon water, like butyrate of baryta.

Hippurate of baryta, $BaO.\overline{Hi} + HO$, is obtained in microscopic, square prisms, and loses its water at 100°.

Hippurate of strontia, $SrO.\overline{Hi} + 5HO$, occurs in broad plates, difficult of solution in cold water, or in microscopic, four-sided prisms, with large terminal planes.

Hippurate of lime, $CaO.\overline{Hi} + 3HO$, occurs in oblique rhombic prisms; it parts with all its water at 100°.

Hippurate of magnesia, $MgO.\overline{Hi} + 5HO$, crystallises in wart-like masses, is readily soluble, and at 100° loses only 4 atoms of water.

Hippurate of cobalt, $CoO.\overline{Hi} + 5HO$, occurs in rose-coloured wart-like masses, consisting of microscopical, flat, four-sided prisms; at 100° it loses all its water, and it is perfectly insoluble in alcohol.

Hippurate of nickel, $NiO.\overline{Hi} + 5HO$, forms apple-green crusts, dissolves in warm spirit, and at 100° loses all its water.

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* Ann. d. Ch. u. Pharm. Bd. 54, S. 29-51. [Schwartz has published another memoir on this acid during the last few months (in Ann. d. Ch. u. Pharm. Bd. 75, S. 190.)—G. E. D.]

Hippurate of copper, $CaO.\overline{Hi}+3HO$, occurs in blue, oblique rhombic prisms, and at 100° is anhydrous.

Hippurate of lead, $PbO.\overline{Hi}$, crystallises from hot solutions with 2 atoms of water in fine silky tufts of needles; from cold solutions, by slow evaporation, in broad four-sided tablets, with 3 atoms of water. At 100° it is anhydrous.

Hippurate of silver, $AgO.\overline{Hi}+HO$, occurs as a curdy precipitate, which dissolves in boiling water, and, on cooling, separates in beautiful silky needles.

Hippurate of iron occurs as a dingy, voluminous precipitate, which does not dissolve, but fuses in boiling water; it dissolves in warm alcohol, but falls as an amorphous precipitate on cooling; it crystallises from the cold solution in oblique rhombic prisms.

Hippurate of oxide of ethyl, $C_4H_5O.C_{18}H_8NO_5$, forms long, white, silky needles, with a greasy feeling, devoid of odour, of an acrid taste, slightly soluble in cold, but more so in hot water; it fuses at 44°, solidifying again at 32°, and on exposure to a stronger heat it decomposes.

Products of its metamorphosis.—The non-nitrogenous acid, $C_{18}H_7O_7.HO$, obtained from hippuric acid by the action of nitrous acid, is, according to Strecker, readily soluble in ether, yields with baryta a salt, crystallising in silky needles, and readily soluble in water, and with oxide of silver a salt, $AgO.C_{18}H_7O_7$, which dissolves in boiling water, and on cooling crystallises in delicate needles; and which, on exposure to heat, developes hydride of benzoyl. The production of this acid from hippuric acid is shown in the equation $C_{18}H_8NO_5+3HO-H_3N=C_{18}H_7O_7.HO$.

Preparation.—Hippuric acid is very easily obtained from the urine of horses, but there is some difficulty in separating it from the colouring matter. Fresh urine, obtained from horses, is evaporated to $\frac{1}{8}$th of its volume, and then treated with hydrochloric acid; after it has cooled, the acid which has separated, and is usually much discoloured, is dissolved in ten times its bulk of boiling water, and boiled with milk of lime; the solution is filtered, a solution of alum is added till there is an acid reaction, and the alumina is then precipitated by bicarbonate of soda. The boiling with milk of lime destroys a portion of the pigment adhering to the hippuric acid, while another portion of the pigment is precipitated with the alumina. The acid precipitated by hydrochloric acid from the filtered fluid is again dissolved in boiling water, boiled with animal charcoal, and filtered while hot; on cooling, the acid now separates in a colourless state. Moreover, by mere, but often repeated, boiling of horses' urine, and of the hippuric acid separated from it with milk of lime, we may obtain it free from colour.

Perfectly fresh urine must be used, since horses' urine, even at an ordinary temperature, very soon begins to decompose; and it then no longer yields hippuric but benzoic acid.

Tests.—Hippuric acid presents such characteristic properties, that if it be once pretty well freed from other substances, it can scarcely be confounded with any other acid, except, perhaps, benzoic acid, if the latter be contaminated with organic colouring, and nitrogenous matters; since in the pure state, the two acids act so differently when exposed to heat that it is impossible to confound one with the other.

When they occur in an impure state, they may be distinguished from one another by attention to the following points.

Hippuric acid, which is far less soluble in ether than benzoic acid, crystallises from hot saturated solutions in needles or prisms, while benzoic acid crystallises in scales. The latter often causes such a solidification of the whole fluid, that the vessel after cooling may be inverted without the escape of a single drop. Further, on the addition of acids to solutions of their salts, hippuric acid is at once precipitated in needles or spangles, while benzoic acid gives rise to a milky turbidity before it crystallises. On rapidly evaporating an acid fluid in a basin covered over with paper, delicate glistening scales may be observed on its lower surface if benzoic acid be present, but not if hippuric acid alone be present in the fluid. The microscope, however, affords the best means of distinguishing these acids from one another, by comparing their crystalline forms in accordance with the directions given in pp. 83, and 188. With such an examination, it is impossible that these acids can be confounded.

In order to detect small quantities of hippuric acid in animal fluids, we must be especially careful that such fluids are fresh, since if this be not the case, the hippuric acid will have become changed into benzoic acid, which on evaporation for the most part escapes with the aqueous vapour; if, however, the animal fluid be still perfectly undecomposed, it must be evaporated to almost the consistence of a syrup and then extracted with alcohol of specific gravity, 0.83; a little oxalic acid must be added to the alcoholic extract during its evaporation, which must be continued till it assumes a syrupy consistence; the residue must then be extracted with ether to which $\frac{1}{6}$th of its volume of alcohol has been added. This extract must now be carefully evaporated, and the residue which, besides free acids, also contains fatty matters, must be treated with water in in order to remove the latter. It sometimes happens that on the addition of the water, crystals of hippuric acid at once separate from the above extract-like mass; but whether this be the case or not, this ethereal extract must be warmed with water, and allowed to percolate through a previously well moistened filter; the filtered acid fluid may then either be gently concentrated by warmth, or, if its quantity be very small, it may be left to spontaneous evaporation in a watch-glass; crystals of hippuric acid very soon separate, whose form must be determined by the microscope. If much hippuric acid be present, it will sometimes separate from the syrupy residue by the mere addition of hydrochloric acid, and can be distinguished from uric acid and other crystalline substances by the microscope.

Physiological Relations.

Occurrence.—Hippuric acid was first recognised by Liebig as an independent acid in *horses' urine* where it had previously been mistaken for benzoic acid; it has been subsequently found in the urine of many graminivorous animals, as, for instance, oxen, elephants, goats, hares, sheep, &c. It is, however, singular that, according to Wöhler, it is entirely absent in the urine of calves while suckling, although the fluid contains allantoine, uric acid, and urea, (see p. 176.) In the urine of the pig neither Boussingault,* nor von Bibra,† could discover any hippuric acid. Liebig‡ was the first who recognised its presence in healthy human urine, in which it principally occurs after the use of vegetable food: according to him it exists in human urine, in about the same quantity as uric acid, while according to Bird,§ the hippuric acid most commonly stands to the uric acid in the ratio of 1 : 3.

I have already remarked in p. 83. that benzoic acid never occurs in fresh horses' urine, and that it is merely a product of the decomposition of that fluid; I can, however, perfectly confirm the observation of Schmidt,‖ that hippuric acid is occasionally, although very rarely, entirely absent, and that in its place there is found an oily matter which when heated with caustic alkalies yields benzine.

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* Ann. de Chim. et de Phys. 3 Sér. T. 15, pp. 97-104.

† Ann. de Ch. u. Pharm. Bd. 53, S. 98-112.

‡ Ibid. Bd. 37, S. 257.

§ London Medical Gazette, vol. 34, p. 685: [In his Urinary Deposits, &c. 3rd edit., p. 96, this opinion is considerably modified. We there find that "its quantity in health is not constant, and always, unless after the ingestion of benzoic or cinnamic acid, very much less than has been stated."—G. E. D.]

‖ Entwurf u. s. w. S. 39.

Attempts have been made to refute Liebig's assertion that hippuric acid always exists in human urine, at least after the use of vegetable food; but although I formerly did not succeed in detecting this acid in my own urine during a purely vegetable diet, I have since very frequently convinced myself, both from experiments both on large and on small quantities of urine, that this acid is constantly present during the use of a mixed diet. The presence of hippuric acid may, however, readily escape our notice if we evaporate the acid urine too rapidly, after the acid has been converted into benzoic acid; on the other hand, we need be under no apprehension that the hydrochloric acid which is added will decompose the hippuric acid, as in order to effect any change on it, a very concentrated acid and prolonged boiling are required.

Hippuric acid is not found in the urine of *carnivorous animals*, but it has probably not been sought for with sufficient care and attention. In the urine of tortoises neither J. Müller and Magnus,* nor Marchand† could detect hippuric acid; I have, however, convinced myself with the greatest certainty, and on many occasions, that hippuric acid is present in addition to uric acid in the urine of *Testudo græca*.

Magnus was unable even to find uric acid in the urine of *Testudo nigra s. elephantopus*, while Marchand found uric, but no hippuric acid in the urine of *T. tabulata;* I probably worked with much larger quantities, and certainly always used fresh urine. My specimens of *Testudo græca* were fed with lettuce and other vegetables. The urine may be easily collected by placing the animal on its back in a dish; when the bladder is moderately filled, the animal very soon spontaneously passes its urine, which, besides alkaline urates and hippurates, contains free hippuric acid. Without the preliminary addition of a stronger acid, we may obtain the hippuric acid in a crystalline state by the addition of water to the ethereal extract, and sufficiently pure to admit of our accurately studying its behaviour when exposed to heat, its solubility, &c.; if, however, oxalic or hydrochloric acid were used in the process, in the manner which has been already explained, we should obtain much larger quantities of hippuric acid.

In *morbid human urine* I have almost always been able to detect hippuric acid; it especially occurs in large quantity in acid *febrile urine*, whether the fever be typhus or be associated with pneumonia or any other pathological process. Before hippuric acid was discovered in healthy human urine, I detected its presence in *diabetic urine*,* in which it is more easily recognised than in other forms of urine which abound in extractive matters.

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* Müller's Archiv. 1835. S. 214.

† Journ. f. pr. Ch. Bd. 34. S. 244-247.

In diabetic urine I have found hippuric acid in every instance in which I have sought for it; Ambrosiani, Hünefeld, and others have also found it in the urine during this disease; Bouchardat found it in a case of what is called *diabetes insipidus;* Pettenkofer† found it in large quantity in the urine of a girl with chorea. In the case of a drunkard with a contracted, probably a hob-nail, liver, Bird‡ observed a sediment consisting of hippuric acid, on the addition of hydrochloric acid to the concentrated urine. In the strongly acid urine which is sometimes passed in fevers, the acid reaction is in a great degree dependent on the hippuric acid; from the ethereal extract of urine of this nature, and without the preliminary addition of any acid, we often obtain the most beautiful crystals of hippuric acid. Such urine is, however, by no means so common as is generally supposed; for this febrile urine is much more rapidly rendered acid by lactic acid, (which is not formed till after the emission of the urine,) than the normal secretion, and hence, unless it be examined when perfectly fresh, we usually find that febrile urine is more acid than the normal fluid. I have not been able to establish any relation between certain morbid processes or groups of symptoms and the amount of the hippuric acid contained in the urine.

Hippuric acid has as yet been found nowhere but in the urine. [Its recent discovery in the blood of oxen, by Verdeil and Dollfass,§ is noticed in the second volume, in the article on "The Blood."—G. E. D.]

Origin.—Notwithstanding the many points which seem to elucidate the inquiry, the formation of hippuric acid in the animal body still remains unexplained. All views regarding the chemical constitution of hippuric acid coincide in the belief that it contains, hidden within it, a benzoyl-compound ($C_{14}H_5O_2 + H$ or $+ O$ or $+ H_2N$); it is an established fact that benzoic acid, oil of bitter almonds, and cinnamic acid, which is very similar to benzoic acid, are transformed in the animal body into hippuric acid. Now, since the benzoyl-compounds are almost entirely confined to the vegetable kingdom, we might believe that this constituent of hippuric acid principally arises from vegetable food, and the abundance of this acid in the urine of many herbivorous animals is in favour of this view. We might therefore be led to regard one constituent of hippuric acid as an immediate product of decomposition of certain constituents of food, namely, of the vegetable portion; but this view is opposed by several positive experimental results; thus in the urine of patients on an antiphlogistic diet, who for several days have scarcely taken any food, the amount of hippuric acid is actually increased.

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* Journ. f. pr. Ch. Bd. 6, S. 113.

† Ann. d. Ch. u. Pharm. Bd. 57, S. 128.

‡ London Medical Gazette, vol. 34, p. 686.

§ [Compt. rend. T. 29, p 789; and more fully in the Ann. d. Ch. u. Pharm. Bd. 74, S 214.]

The urine of tortoises, which had been kept fasting for more than six weeks, still contained hippuric acid; and it occurred in the urine of diabetic patients who were restricted to a purely animal diet. In the urine of granivorous birds, as well as in that of the larva of *Sphinx Cossus*, and of several other herbivorous insects, I have found, after careful examination, larger or smaller quantities of uric acid, but no hippuric acid. Hence we may conclude in the first place that the formation of uric acid is not dependent on the use of animal food, or that of hippuric acid on the use of vegetable food, and secondly, that the latter acid must derive its nitrogenous constituent from the retrograde metamorphosis of the animal tissues. This is, moreover, not opposed to our chemical facts in relation to the production of the benzoyl-compounds, for there is every reason to believe that the nitrogenous tissues which, according to the admirable investigations of Guckelberger, when treated with oxidising agents, yield benzoic acid and benzonitrile, yield a like product of decomposition during the gradual oxidation which they undergo in the animal body.

In reference to the nitrogenous constituent of hippuric acid we may regard it as fumaramide, or as glycine; it is undoubtedly derived from the animal albuminous substances, and probably from effete tissue. It would, however, certainly be rash to attribute it principally to the decomposition of the gelatigenous tissues, simply because it is chiefly formed from them in artificial experiments; but independently of the circumstance that this product into which the nitrogenous adjunct of hippuric acid becomes converted, may also be obtained from albuminous substances, we must bear in mind that the metamorphosis going on in the gelatigenous tissues is certainly too insignificant to account for the quantity of hippuric acid found in the urine, (as, for instance, after the ingestion of from two drachms to half an ounce of benzoic acid,) and that the same substance is separated even more abundantly from the liver. Glycine must therefore be regarded in the same light as urea, as a common product of decomposition of nitrogenous substances.

We cannot therefore find any very immediate source from which either of the proximate constituents of this acid can be derived, since neither physiological nor pathological relations elucidate the process by which it is formed in the animal body.

This much, however, is certain, that hippuric acid is to be regarded merely as a product of excretion, and consequently that it can have no special uses in the animal organism.

It is to be regretted that benzoic acid is so rarely prescribed by the physician; and that, even in those cases, it is usually ordered on most irrational principles. It deserves to be thoroughly tested in a pharmacological point of view; it certainly possesses one great advantage over all the other officinal acids in its property of rendering the urine strongly acid. Ure attaches great importance to this circumstance, but it does not appear to have been turned to much account in actual practice.

URIC ACID.—$C_5HN_2O_2.HO$.

Chemical Relations.

Properties.—Pure uric acid occurs either in a glistening white powder, or in very minute scales, which under the microscope are seen to consist of irregular plates, whose crystalline form (see our remarks on the crystals, in the consideration of the "Tests,") cannot very well be made out: it is a substance devoid of odour and taste; it requires 1800 or 1900 parts of hot, and 14000 or 15000 parts of water at the ordinary temperature of 20°, to dissolve it; it is insoluble in alcohol and ether, and does not redden litmus. It dissolves in concentrated hydrochloric acid somewhat more readily than in water; it dissolves tolerably freely, and without decomposition, in concentrated sulphuric acid, but is again precipitated on the addition of water. It dissolves readily in the alkaline carbonates, borates, phosphates, lactates, and acetates, since it abstracts some of the alkali from these salts, and is thus rendered more soluble. Uric acid is expelled from all its salts by acetic as well as by other acids, and on its separation at first forms a gelatinous mass, (according to Fritzsche,* a hydrate $= C_5HN_2O_2.HO + 4HO$) which, however, soon changes into small glistening plates.

Uric acid belongs to the *weakest class of acids*; thus, as in the case of the fatty acids, it does not directly expel carbonic acid from carbonate of potash, but urate of potash and bicarbonate of potash are formed, if a sufficient amount of uric acid be added; if the solution of potash be concentrated, the urate of potash remains undissolved; the behaviour of uric acid to the alkaline borates and phosphates is similar, with the exception of this difference, that the solution of phosphate of soda, which has an alkaline reaction, reddens litmus when an excess of uric acid has been added to it, in consequence of the formation of biphosphate of soda.

Uric acid, when submitted to *dry distillation*, is converted into urea, cyanic acid, cyamelide, hydrocyanic acid, and a little carbonate of ammonia, leaving, as a residue, a brownish-black coal, rich in nitrogen.

On fusing uric acid with *hydrated potash*, carbonate and cyanate of potash, with cyanide of potassium, are formed. On boiling uric acid with 20 parts of water, and adding peroxide of lead as long as the brown colour of the oxide continues to disappear, there are formed oxalate of lead, urea, and allantoine, ($2C_5HN_2O_2.HO + 2O + 3HO = C_2H_4N_2O_2 + 2C_2O_3 + C_4H_3N_2O_3$).

Moist uric acid, placed in *chlorine gas*, intumesces, and, giving off carbonic and cyanic acids, is converted into oxalic acid and hydrochlorate of ammonia; dry uric acid in dry chlorine gas yields much cyanic acid, chloride of cyanogen, and hydrochloric acid, leaving only a small carbonaceous residue. Uric acid dissolves with considerable readiness in dilute *nitric acid*, developing equal volumes of nitrogen and carbonic acid, and yielding to the solution several of the different products of decomposition which we shall presently describe. On evaporating to dryness a solution of uric acid in nitric acid, there is left a red amorphous residue, which, especially if we expose it to the vapour of ammonia, assumes a very beautiful purple tint; on moistening the red mass (murexide) with a little caustic potash, a beautiful violet tint is developed (Schlossberger.†)

Composition.—According to the above formula, deduced by Bensch‡ from his analyses of the urates, uric acid consists of:

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* Bull. scient. de St. Petersb. T. 1, Nos. 79 et 107.

† Arch. f. physiol. Heilk. Bd. 8, S. 294.

‡ Ann. d. Ch. u. Pharm. Bd. 51, S. 189-208.

Carbon	5 atoms	35·714
Hydrogen	1 „	1·191
Nitrogen	2 „	33·333
Oxygen	2 „	19·048
Water	1 „	10·714
		100·000

The atomic weight of the hypothetical anhydrous acid = 937·5, and its saturating capacity = 10·656. There is hardly any other organic acid, whose products of decomposition have been so accurately and so generally examined as those of uric acid, and yet chemists have been unable to establish for it any rational formula. Bensch's discovery of the true atomic weight of uric acid has tended to weaken the views which were previously held regarding the intimate constitution of this acid. If we choose to double the atoms, and if we so far extend the idea of conjugation, that the conjugating substances may, in their union, lose certain atoms of hydrogen and oxygen, (so that we might regard oxamide as a body composed of oxalic acid and ammonia, and benzanilide as composed of benzoic acid and aniline,) then indeed, much might be explained at which we could not arrive by a strict logical induction. Taking into consideration those substances which for a long time have been regarded as conjugated, it seems that we should only consider as true conjugated bodies those compounds in which two organic bodies unite with one another, the union being accompanied with a loss of water; which, however, in some cases may be shewn by direct experiment, and in others, may be assumed with great probability, to lie without the true atomic group, and may therefore be regarded as a basic, acid, or saline atom of water. Many of the substances which have been recently regarded as conjugated bodies, undoubtedly contain certain atoms of oxygen and hydrogen less than the anhydrous substances from which they are produced, or may be supposed to be produced; but this view does not coincide with the original idea of a conjugated body; especially when it is probable that in this union one of the substances has contributed the oxygen and the other the hydrogen for the formation and separation of the water.

It would be equally injudicious, were we not to facilitate the recognition of the metamorphosis or transposition of the atoms of organic substances, by some general remarks on the connection and separation of atoms.

Such remarks, however, are not based on anything more than a fiction, and do not rest on a conclusion obtained by induction.

That such hypotheses are not always to be rejected in the natural sciences, is shown by Newton's hypothesis of emanating rays of light, which now, indeed, is entirely displaced by the undulatory theory. In this light we must consider the view regarding the composition of uric acid, put forth some years ago by Liebig and Wöhler. From the decomposition of uric acid by peroxide of lead, they deduced, for uric acid, the hypothetical formula, $C_2H_4N_2O_2+2C_4NO_2$; that is to say, they regarded urea as existing preformed in it, together with an acid incapable of isolation in an undecomposed state, to which they applied the name of *urilic acid.* Now that the substratum of this hypothesis has been more than shaken by the discovery of the true atomic weight of uric acid, we may yet make use of this fiction in order to be able to represent the formation of the products enumerated by Liebig and Wöhler in their classical investigations regarding uric acid. Thus we may conceive, that on the decomposition by peroxide of lead, 2 equivalents of hydrated uric acid contain 1 equivalent of urea, which is isolated, while the 2 equivalents of urilic acid are, in the first place, decomposed into C_4O_4 and C_4N_2, of which the former assimilates 2 atoms of oxygen, and forms oxalic acid, while the latter assimilates 3 atoms of water, and produces allantoine. In a similar way we can elucidate the mode of formation of those numerous products which result from the action of nitric acid on uric acid.

Combinations.—It is only with the fixed alkalies that uric acid forms salts which possess even a moderate degree of solubility; the lithia-salt is especially soluble, while urate of ammonia is almost insoluble. Potash and soda are the only bases with which uric acid forms neutral salts; with ammonia and all other bases it forms only acid and insoluble salts. On passing carbonic acid into a potash-solution of uric acid, an acid potash-salt is precipitated.

Neutral urate of potash, $KO.C_5HN_2O_2$, is obtained on mixing alcohol with a solution of uric acid in potash (free from the carbonate) and concentrating the solution. It crystallises in needles free from water, dissolves in 30 or 40 parts of boiling water, slightly in alcohol, and not at all in ether, has a strong alkaline reaction, and attracts carbonic acid from the atmosphere.

Bi-urate of potash, $KO.C_5HN_2O_2+HO.C_5HN_2O_2$, is precipitated by carbonic acid from the solution of the neutral salt; it crystallises in needles, dissolves in 70 or 80 parts of boiling water, and in 700 or 800 parts of water at 20°. The solution does not exhibit an alkaline reaction, and is precipitated by hydrochlorate of ammonia and the alkaline bicarbonates.

Neutral urate of soda, $NaO.C_5HN_2O_2+HO$ crystallises in wart-like masses, dissolves in 80 or 90 parts of boiling water, is slightly soluble in alcohol, and insoluble in ether; at 100° it loses its water of crystallisation.

Bi-urate of soda, $NaO.C_5HN_2O_2+HO.C_5HN_2O_2+HO$ crystallises in short hexagonal prisms, or in thick six-sided (microscopic) tablets, which commonly arrange themselves in star-formed masses in which the individual crystals are larger and can be more distinctly made out than in the microscopic aggregations of the ammonia-salt; it begins to lose its water of crystallisation at 170°, and is soluble in 124 parts of boiling and 1150 parts of cold water.

Bi-urate of ammonia, $H_4NO.C_5HN_2O_2+HO.C_5HN_2O_2$, may be obtained crystallised in extremely delicate needles, but it also forms under the microscope, globular opaque masses, from some points of which extremely delicate spikelets may be seen to project.

Almost all the other salts of uric acid occur as amorphous precipitates, and consist of 1 atom of base and 2 atoms of uric acid, of which 1 atom always retains its basic atom of water; hence we cannot well assume that the atomic weight of uric acid should be doubled, (that is to say $=C_{10}H_2N_4O_4$) for if, with such an atomic weight, these salts were all neutral salts, they, or at all events, some of them, would certainly lose this 1 atom of water at a higher temperature.

The salts of *baryta*, *strontia*, and *lime*, are represented by the formula $RO.C_5HN_2O_2+HO.C_5HN_2O_2+HO$.

Bi-urate of magnesia, $MgO.C_5HN_2O_2+HO.C_5HN_2O_2+6HO$, crystallises in delicate needles, loses 5 of its 6 atoms of water at 170°, and dissolves in 160 parts of boiling water, but in not less than 3800 parts of cold water.

Bi-urate of lead, $PbO.C_5HN_2O_2+HO.C_5HN_2O_2+HO$, is a white powder, which loses its water of crystallisation at 160°.

Bi-urate of copper, $CaO.C_5HN_2O_2+HO.C_5HN_2O_2+5HO$, is a green powder which, at 140°, loses 3 atoms of water of crystallisation.

Sulphate of uric acid, $HO.C_5HN_2O_2+4\,(HO.SO_3)$, is formed by dissolving uric acid in warm concentrated sulphuric acid, from which, on cooling, it separates in colourless crystals, which fuse at 70°, in cooling again solidify in a crystalline mass, and become decomposed at 170°; it attracts water from the atmosphere, and thus becomes decomposed into its proximate constituents in the same manner as if water were added to it.

Products of its metamorphosis.—The products of decomposition of uric acid are of extreme interest, insomuch as they afford us a deep and general insight into the various transpositions of atoms and atomic groups.

Alloxan, erythric acid, $C_8H_4N_2O_{10}$, is produced when 1 part of dry uric acid is gradually introduced into 4 parts of nitric acid of 1.42 to 1.53 specific gravity, when the whole finally solidifies and becomes crystalline. A better method of preparing this body is by mixing 4 parts of uric acid with 8 parts of moderately strong hydrochloric acid, and then gradually introducing 1 part of chlorate of potash into the fluid; in the latter case, urea and alloxan are formed without any development of gas, while in the former case, nitrogen and carbonic acid are evolved in consequence of the decomposition of the urea by nitrous acid. (Compare p. 154.)

Alloxan crystallises in large colourless rhombic octohedra (which at first have a diamond-like lustre, but soon effloresce) with 6 atoms of water of crystallisation from hot but not perfectly saturated solutions; while from saturated solutions it crystallises in anhydrous four-sided prisms: it has a faintly saline taste, a sickly odour, reddens litmus, and communicates a purple red colour to the skin.

It is easy to see that in accordance with the above fiction respecting urilate of urea, urilic acid assimilates 4 atoms of water and 2 atoms of oxygen, and thus forms alloxan, ($C_8N_2O_4+4HO+2O=C_8H_4N_2O_{10}$.)

Alloxanic acid, $C_4HNO_4.HO$, is formed by digesting alloxan with caustic alkalies, and by decomposing the baryta-salt by sulphuric acid. It crystallises in concentrically grouped needles, which are unaffected by exposure to the atmosphere, have an acid, (but subsequently leave a sweetish) taste, dissolve readily in water, less in alcohol, and very slightly in ether; this acid reddens litmus strongly, decomposes carbonates and acetates, and oxidises zinc and cadmium, hydrogen being at the same time developed; in an aqueous solution it becomes decomposed at a temperature above 60°. Its alkaline salts are soluble in water and crystallisable; its other neutral salts are difficult of solution: like uric acid it has a strong tendency to form acid salts, all of which are soluble (Schlieper.)*

Alloxanic acid is produced by the abstraction of 2 atoms of water from alloxan.

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* Ann. d. Ch. u. Pharm. Bd. 55, S. 251-297.

If a solution of alloxanic acid be submitted to prolonged ebullition, it evolves carbonic acid, and is decomposed into an acid insoluble in water, *leucoturic acid*, $C_6H_3N_2O_6$, and into a soluble indifferent body, *diffluan;* $C_6H_4N_2O_5$ (Schlieper.)

Two atoms of alloxan yield 1 atom of this new acid, and 1 atom of diffluan, besides 4 atoms of carbonic acid and 1 atom of water, for $C_{16}H_8N_4O_{20}=C_6H_3N_2O_6+C_6H_4N_2O_5+4CO_2+HO$.

Mesoxalic acid, C_3O_4, is produced together with urea, when a solution of alloxan is added by drops to a boiling solution of acetate of lead: it is crystallisable, and reddens litmus.

Alloxan becomes simply decomposed into 1 equivalent of urea and 2 equivalents of mesoxalic acid, for $C_2H_4N_2O_2+2C_3O_4=C_8H_2N_2O_{10}$.

Mykomelinic acid, $C_8H_5N_4O_5$, is formed when an excess of dilute nitric acid is added to a supersaturated solution of alloxan, and boiled for some time with ammonia; in its moist state it occurs as a yellow gelatinous mass; when dried, it is a yellow powder, which is soluble in water, reddens litmus, and decomposes carbonates.

This acid is formed from 1 atom of alloxan and 2 atoms of ammonia with the separation of 5 atoms of water; $C_8H_4N_2O_{10}+2H_3N-5HO=C_8H_5N_4O_5$.

Parabanic acid, $C_6N_2O_4+2HO$, is prepared by digesting 1 part of uric acid or of alloxan, with 8 parts of moderately diluted nitric acid, and evaporating the solution to the consistence of a syrup; after some time there is a separation of small plates or minute prisms of parabanic acid; it is unaffected by exposure to the atmosphere, has an acrid, sour taste, dissolves readily in water, fuses when heated, and partially sublimes without decomposition.

Parabanic acid is produced in the following manner from uric acid and nitric acid: the urea of the uric acid is decomposed as usual by the nitrous acid which is formed, but 2 atoms of water and 4 atoms of oxygen enter into combination with the urilic acid with which they form 2 atoms of carbonic acid, and 1 atom of parabanic acid, for $C_8N_2O_4+H_2O_2+4O-C_2O_4=C_6N_2O_4+2HO$.

Alloxan with 2 atoms of oxygen becomes decomposed into 2 atoms of carbonic acid, 4 atoms of water, and 1 atom of parabanic acid, for $C_8H_4N_2O_{10}+2O=C_2O_4+H_4O_4+C_6N_2O_4$.

Hydrurilic acid, $C_{12}H_3N_3O_9+2HO$, is formed at the same time with alloxan under certain conditions not yet accurately understood; it occurs as a white flocculent powder, consisting of delicate needles; it is difficult of solution in cold, but dissolves more readily in hot water; it is insoluble in alcohol; with the alkalies it forms acid and neutral salts; this acid may be regarded as a combination of the above mentioned hypothetical urilic acid with water; 3 atoms of urilic acid and 10 atoms of water forming 2 atoms of hydrurilic acid. By nitric acid, this acid is converted into nitrohydrurilic acid, $C_8H_2N_3O_{14}$.

Oxaluric acid, $C_6H_3N_2O_7.HO$: if a solution of uric acid in dilute nitric acid be supersaturated with ammonia and evaporated, the ammonia-salt of this acid separates in needles; on separating the acid from the salt by means of a more powerful acid we obtain it as a glistening white crystalline powder with an acid taste and an acid reaction; when heated it becomes decomposed into 2 atoms of oxalic acid and 1 atom of urea, for $C_6H_3N_2O_7.HO=2C_2O_3+C_2H_4N_2O_2$.

Crystallised oxaluric acid may therefore be regarded as a combination of 2 atoms of oxalic acid and 1 atom of urea, for $C_4O_6+C_2H_4N_2O_2=C_6H_4N_2O_8$.

Parabanic acid when boiled with ammonia takes up 3 atoms of water, and forms *oxaluric acid,* for $C_6N_2O_4+H_3O_3=C_6H_3N_2O_7$.

Thionuric acid, $C_8H_7N_3S_2O_{14}$, is formed by mixing a solution of alloxan with an excess of aqueous sulphurous acid, supersaturating with ammonia and boiling for some time; as the solution cools, *thionurate of ammonia* separates in nacreous crystalline scales; on combining the acid of this salt with lead, decomposing the lead-salt by sulphuretted hydrogen, and evaporating the filtered fluid, we obtain *thionuric acid* in the form of a white crystalline mass with an acid taste, which is unaffected by exposure to the air, dissolves readily in water, and is decomposed both by simple boiling and on the addition of acids. The salts of this acid saturate 2 atoms of base; on the addition of concentrated sulphuric acid, sulphurous acid is developed.

Thionuric acid may be regarded as a combination of 1 atom of alloxan with 1 atom of ammonia and 2 atoms of sulphurous acid, for $C_8H_4N_2O_{10}+H_3N+S_2O_4=C_8H_7N_3S_2O_{14}$.

Uramile, $C_8H_5N_3O_6$, is produced either by simply exposing thionuric acid to ebullition, or by treating thionurate of ammonia with an excess of hydrochloric acid; it forms minute, silky, glistening needles, and on exposure to the atmosphere and to warmth, assumes a rose-red tint. It is insoluble in cold water and only dissolves slightly in boiling water; the caustic alkalies and concentrated sulphuric acid dissolve, but do not decompose it: by simple ebullition, however, its solutions become decomposed. The alkaline solution of uramile on exposure to the air assumes a purple red tint, and deposits green crystals with a metallic lustre.

On simply boiling *thionuric acid*, 2 atoms of *sulphuric acid* are given off, and *uramile* is formed; for $C_8H_7N_3S_2O_{14} - 2SO_3.HO = C_8H_5N_3O_6$.

Uramile may be regarded as uric acid in which the urea is replaced by 1 atom of ammonia and 2 atoms of water; it is, therefore, hypothetically composed of 1 atom of urilic acid, 1 atom of ammonia, and 2 atoms of water, for $C_8N_2O_4 + H_3N + 2HO = C_8H_5N_3O_6$.

Uramilic acid, $C_{16}H_{10}N_5O_{15}$, is formed by boiling uramile either with a solution of potash or with dilute acids; it crystallises in colourless, four-sided prisms, or silky, glistening needles, is soluble in water, faintly reddens litmus, dissolves without the development of gas, or the communication of colour, in sulphuric acid; is decomposed by nitric acid, and forms soluble salts only with the alkalies.

Acids and alkalies expel 1 atom of ammonia from 2 atoms of uramile, which, in its place, receive 3 atoms of water; $C_{16}H_{10}N_6O_{12} - H_3N + 3HO = C_{16}H_{10}N_5O_{15}$.

Alloxantin, $C_8H_5N_2O_{10}$, is formed by boiling 1 part of uric acid with 32 parts of water, then gradually adding dilute nitric acid, and finally evaporating the fluid to one third of its volume: after some time crystals of alloxantin separate themselves. It is prepared from alloxan by the action of reducing bodies, as for instance, sulphuretted hydrogen, or hydrochloric acid and zinc. It crystallises in oblique four-sided prisms, which at first are colourless, but on exposure to the air become yellowish, and if acted on by the vapour of ammonia, become red. It is slightly soluble in cold, but dissolves readily in hot water, it reddens litmus, and is converted by chlorine into alloxan; with baryta-water it gives a violet-coloured precipitate.

When very dilute nitric acid acts on uric acid, the urilic acid takes up 1 atom of oxygen from the nitric acid and 5 atoms of water in order to form alloxantin ($C_8N_2O_4 + O + 5HO = C_8H_5N_2O_{10}$), while the hyponitric acid which is formed, becoming decomposed into nitrous and nitric acids, partly combines with and partly decomposes the urea of the uric acid.

On treating alloxan with sulphuretted hydrogen, the sulphur separates, while the hydrogen unites with the alloxan, and forms alloxantin, $C_8H_4N_2O_{10} + H = C_8H_5N_2O_{10}$.

Murexide, $C_{12}H_6N_5O_8$, *purpurate of ammonia*, may be obtained by several very different methods. The most simple means of preparing it is by boiling equal parts of uramile and red oxide of mercury with 40 parts of water and a very small quantity of ammonia; the purple-red fluid which is thus obtained must be filtered, and after standing some time will deposit crystals of murexide. This body may also be prepared by dissolving uric acid in dilute nitric acid, and evaporating the fluid till it assumes a reddish tint; after it has cooled to 70° it must be saturated with dilute ammonia, diluted with half its volume of water, and allowed to stand.

Murexide crystallises in short four-sided prisms, two of whose surfaces present a cantharides-green, glistening appearance: in refracted light these crystals present a garnet-red tint; when pulverised it is of a brownish-red colour, and under the burnishing rod presents a green, metallic lustre; it is insoluble in alcohol and ether, slightly soluble in cold, but freely in hot water, and it dissolves in a solution of potash, communicating an indigo-blue colour to the fluid. It is decomposed by all the mineral acids.

In the preparation of *murexide* from *uramile* and *red oxide of mercury*, 2 atoms of uramile take up 3 atoms of oxygen from the mercury, and form 1 atom of *murexide*, 1 atom of *alloxanic acid* and 3 atoms of *water*; ($C_{16}H_{10}N_6O_{12} + 3O = C_{12}H_6N_5O_8 + C_4HNO_4 + 3HO$.)

When uric acid is dissolved in dilute nitric acid, the principal product is alloxantin, which by the action of the nitric acid during evaporation is in part converted into alloxan, from which murexide is formed on the addition of ammonia; for 1 atom of *alloxan*, 2 atoms of alloxantin, and 4 atoms of ammonia, yield 2 atoms of *murexide* and 14 atoms of *water*; ($C_8H_4N_2O_{10} + C_{16}H_{10}N_4O_{20} + H_{12}N_4 = C_{24}H_{12}N_{10}O_{16} + H_{14}O_{14}$.)

Murexan, $C_6H_4N_2O_5$, *purpuric acid*, is prepared by dissolving murexide in a solution of potash, boiling, and supersaturating with dilute sulphuric acid; it crystallises in silky, glistening scales, is insoluble in water and in dilute acids, but dissolves unchanged in concentrated sulphuric acid; it likewise dissolves in the alkalies, without, however, neutralising them.

On treating murexide with alkalies or with acids, 2 atoms of *murexide* take up 11 atoms of *water*, and are converted into 1 atom of *alloxan*, 1 atom of *alloxantin*, 1 atom of *murexan*, 1 atom of *urea*, and 2 atoms of *ammonia*; ($C_{24}H_{12}N_{10}O_{16} + H_{11}O_{11} = C_8H_4N_2O_{10} + C_8H_5N_2O_{10} + C_6H_4N_2O_5 + C_2H_4N_2O_2 + H_6N_2$.)

Preparation.—The best method of preparing uric acid is that given by Bensch. The excrements of serpents or birds, or calculi of uric acid, are boiled in a solution of 1 part of hydrate of potash in 20 parts of water till ammoniacal fumes cease to be evolved. A current of carbonic acid is now passed through the solution till the fluid almost ceases to have any alkaline reaction; the precipitated urate of potash is washed with cold water till it begins to dissolve; on now dissolving this potash-salt in a solution of potash, warming it, and pouring it into an excess of warmed hydrochloric acid, we obtain a precipitate of pure uric acid.

Tests.—Uric acid possesses such characteristic properties, and differs in so many respects from all other substances occurring in the animal body, that it can hardly be confounded with any other substance, unless possibly with xanthine and guanine (see p. 169 and p. 171); and from these it may be distinguished with extreme readiness and certainty, by the relation of its alkaline salts towards carbonic acid and the alkaline bicarbonates. Uric acid is, however, principally distinguished from all other organic substances (except perhaps from caffeine) by the murexide test, that is to say, by the purplish red residue which its solution in nitric acid leaves on evaporation; the further addition of caustic potash should, however, never be omitted, by which a yet more distinct reaction —the development of a splendid violet tint—is induced.

All chemical means would, however, frequently fail, and the presence of uric acid would remain undetected, where the quantity of matter to be examined is so small as to afford very slight traces of uric acid, if we were not in possession of the microscope, whose use in physiological chemistry is inestimable. No substance presents such characteristic and so easily determinable crystalline forms under the microscope as uric acid, or crystallises so readily. Hence it may be detected with ease and certainty by all who are moderately familiar with the use of the microscope, and with the various forms which the crystals of uric acid present. Although, to beginners, the form of the crystals of uric acid appears truly protean, yet with some knowledge of crystallography one form may very readily be deduced from another. We must, however, here refer to the admirable analysis of the crystallogenesis and crystallography of uric acid, as given by Schmidt.* For those who are acquainted with crystallography, it is sufficient to give the symbols for the perfect combination of the crystal of uric acid: $\infty\breve{P}2.\ \infty P.\ \infty\bar{P}2.\ \infty\bar{P}\infty.\ 0P.$

For the benefit of those who are unlearned in crystallography, we will remark that uric acid when it gradually and spontaneously separates from urine, appears in most cases in the whet-stone form, that is to say it forms flat tablets, which resemble sections made with the double knife through strongly bi-convex lenses, or rhombic tablets whose obtuse angles have been rounded. As the urinary pigment adheres very tenaciously to the uric acid, it is only rarely that these crystals are devoid of colour; and if we see a crystal presenting an extraordinary form and of a yellow colour, the probability is that it is a crystal of uric acid. On artificially separating uric acid from its salts it often appears in perfect rhombic tablets, and even oftener in six-sided plates (resembling those of cystine); when uric acid crystallises very slowly it forms elongated rectangular tablets or parallelopipeds, or rectangular four-sided prisms, with horizontal terminal planes; the latter are often grouped together in clusters; we also have barrel-shaped or cylindrical prisms, which are composed of the more rarely occurring elliptic tablets; and finally saw-like or toothed crystals, and many derivatives of these forms. If we cannot decide with certainty regarding the presence of uric acid from the form of a crystal, we must dissolve it in potash, place it under the microscope, and add a minute drop of acetic acid; we shall then always obtain one of the more common forms.

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* Entwurf, u. s. w. S. 28-34.

A *quantitative* determination of the uric acid[*] in urine is best made from the residue not taken up by alcohol; by simply treating it with dilute hydrochloric acid, the earths, &c., are got rid of, and nothing but uric acid and mucus remains; their separation may be effected by dissolving them in a dilute solution of potash, from which the uric acid may be precipitated by acetic or hydrochloric acid. The pigment adhering to the uric acid exercises no appreciable influence on the quantitative determination of this substance (Heintz).[†]

To institute a quantitative determination of the uric acid in the blood or any other albuminous fluid is a more difficult and far more precarious operation. For this purpose we take the clear serum and evaporate it to dryness, without previously removing the coagulated albumen by filtration; for if we filtered, the whole process would be very prolonged, as the coagulated serum would become little more than a solid mass of moist coagula, whose thorough washing, even by the addition of much water, would be impossible (see the observations in a future page "on the quantitative determination of albumen.") We now extract the solid residue of the serum with alcohol, and afterwards with hot water; as the uric acid in alkaline fluids, and consequently also in the serum, must be combined with an alkali, it is in the aqueous extract that we must always search for it; during the evaporation of the aqueous extract membranes usually form on the surface of the fluid, which must be removed, but whose removal must slightly affect the accuracy of the analysis; when the aqueous extract has been concentrated to a very small volume, it must be treated with an excess of acetic acid. The uric acid, if its quantity be small, separates very gradually, and unless the acetic acid has been added in great excess, it is usually accompanied with the deposition of a little protein-compound, of whose presence among the crystals of uric acid we can readily convince ourselves by the microscope. It must then be passed through a filter, whose weight has been previously ascertained; and, after careful drying, must be weighed. When the blood is examined qualitatively for uric acid, we must proceed in precisely the same way.

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[*] Journ. f. pr. Ch. Bd. 25, S. 17.

[†] Müller's Archiv. 1846. S. 383-389.

Physiological Relations.

Occurrence.—Uric acid always occurs in the *urine of healthy men*, in the ratio of about one to a thousand parts of urine, as appears from the mean of numerous experiments instituted under different conditions. While living on a mixed diet, the average amount of uric acid which I excreted in 24 hours was 1·183 grammes; according to Becquerel's observations made on 8 different persons, the quantity excreted by healthy men in 24 hours, did not amount to more than from 0·495 to 0·557 of a gramme.

I regret that I must here remark, that the laborious analyses which I made of my own urine cannot altogether serve as standards of comparison for other urines, as when I instituted those observations I was affected with softening of the tissue of the left lung.

Uric acid also occurs in the urine of *carnivorous mammalia*, although generally in far less quantity than in that of man. In the urine of *omnivora*, as, for instance, in that of the pig, neither Boussingault* nor Von Bibra† succeeded in detecting uric acid. In the urine of *graminivorous mammalia* this acid has never been found, except by Brücke‡ [and by Fownes§ G. E. D.], although according to Wöhler it occurs in considerable quantity in the urine of calves, while still sucking, (compare p. 195.) The peculiar urine of birds, both carnivorous and granivorous, and of serpents, (which, as is well-known, is generally discharged with the solid excrements, although in snakes it is often unmixed with the latter,) consists almost entirely of urates. In the urine of *tortoises* uric acid has been found by Marchand* and myself, and Taylor† has discovered it in urinary calculi from the *Iguana*. That the red excrement of *butterflies* consists essentially of alkaline urates, and that the excrement of many *beetles* contains the same substances, has been long known; I have, however, not only found uric acid in the excrements of many *larvæ*‡, but also in large quantities in those vessels of larvæ, to which comparative anatomists have applied the name of biliary vessels.

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* Ann. de Chim. et de Phys. 3 Sér. T. 15, pp. 97-114.

† Ann. d. Ch. u. Pharm. Bd. 53, S. 98-112.

‡ Journ. f. pr. Ch. Bd. 25, S. 254.

§ Phil. Mag. vol. 21, p. 383.

It is well-known that the substance called guano is produced from the excrements of sea-birds; and that it is found not only in the islands of the South Sea (especially in the neighbourhood of Chili,) but also on the coast of Africa and even in England.

In the urine of the lion, Hieronymi§ found only 0·022% of uric acid, and Vauquelin could find none whatever.

The *nature of the food* exerts far less influence on the amount of the uric acid which is secreted than on that of the urea. While living on a mixed diet I‖ discharged on an average 1·1 gramme of uric acid in 24 hours, while during a strictly animal and a strictly vegetable diet, the respective amounts were 1·4 and 1·0 grammes.

As the activity of the skin can to a certain degree replace that of the kidneys, it is easy to understand how an increased activity of the skin may cause a diminution of the uric acid in the urine; hence it was that Fourcroy¶ found that the urine of a man contained more uric acid in winter than in summer, and that Marcet** was led to the conclusion that the uric acid diminishes in the urine after severe perspiration. Schultens†† found that in Holland, where, in consequence of the great humidity of the atmosphere, the cutaneous transpiration is diminished, the amount of uric acid varied from 0·21 to 0·67%; for a similar reason, in tropical countries, lithiasis is altogether unknown. These observations, however, merely show it is impossible to lay down numerically any general standard of comparison.

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* Journ. f. pr. Ch. Bd. 35, S. 244-247.

† Phil. Mag. vol. 28, pp. 36-46.

‡ Jahresb. d. phys. Ch. 1844. S. 25.

§ Jahrb. de Ch. u. Phys. Bd. 3, S. 322.

‖ Journ. f. pr. Ch. Bd. 25, S. 254.

¶ Syst. de Connaiss. chim. T. 10, p. 236.

** An Essay on Calculous Disorders, 1817, p. 176.

†† N. Gehlen's Journ. Bd. 3, S. 4.

Generally, I have only examined the morning urine, in which I have even found as much as 0·878% of uric acid; investigations regarding the relative qualities of the excreted urinary constituents, can only lead to any useful results when they are instituted on one and the same person, and on the whole urine passed in 24 hours for several days in succession. I have endeavoured to arrive at results, in accordance with the above principles, respecting the amount of urine discharged under different conditions, but I have failed in discovering anything further than *that in winter more water is certainly discharged through the urinary bladder, but that in summer, during continuous perspirations, the solid constituents, and especially the uric acid, are neither more nor less than in winter.* It is unnecessary to give the numerical results from which these conclusions were drawn.

There are however other conditions which give rise both to an absolute and a relative augmentation of the uric acid on the urine, and in the first place amongst them we must notice *disturbed* or *imperfect digestion.*

Thus, I have observed both in myself and in several other persons, that if indigestible food or spirituous liquors not sufficiently spiced be taken shortly before bed-time, the morning urine always deposited a considerable sediment. While in the normal state the ratio of the uric acid to the urea=1 : 28 to 30, I found that in urine passed after indigestion, the ratio=1 : 23 to 26, and that the ratio of the uric acid to the other solid constituents, which is ordinarily about=1 : 60 was now=1 : 41 to 52, so that the amount of uric acid is here not only increased at the expense of the urea, but also at that of the other solid constituents of the urine. In the most marked case, I found in 100 parts of solid residue 2·4 of uric acid, 35·2 of urea, and 62.4 of other solid constituents: hence the latter were absolutely increased in this urine.

Consequently it is easy to understand why there is an augmentation of the uric acid in the urine, in many of those cases which the older physicians regarded as *stases* of the portal circulation, hæmorrhoids, and arthritis.

An augmentation in the amount of uric acid in the urine always accompanies the group of symptoms which we are in the habit of designating as fever, the uric acid either separating or remaining dissolved; for no conclusions can be drawn regarding the quantity of uric acid in a specimen of urine, from the formation of a sediment.

I can fully confirm Becquerel's* observations on this point by my own experience.

The sediment which is deposited from acid urine in fever, and in almost all diseases accompanied with severe fever, has long been misunderstood in reference to its chemical composition. Originally it was regarded as a precipitate of amorphous uric acid, and subsequently (and almost to the present time) it was regarded as urate of ammonia. It has, however, been fully demonstrated both by myself† and Heintz‡, that this sediment consists of urate of soda mixed with very small quantities of urate of lime and urate of ammonia. It may be very easily and quickly distinguished from any other urinary sediment, both by the microscope and by the application of a gentle warmth: under the microscope it certainly shows little that is characteristic; it forms fine granules which are sometimes aggregated in irregular heaps, sometimes conglomerated so as to resemble granular cells, and in some instances uniformly distributed over the field of the microscope: as the characteristic forms of uric acid almost immediately appear on the addition of a stronger acid, it is impossible that it can be confounded with any other urinary sediment. An even more simple method of ascertaining that this sediment consists of urate of soda, is afforded by the circumstance that it dissolves at 50°, so that urine rendered turbid by it, when raised to that temperature, becomes clear and limpid.

It would be both superfluous and wearisome to recapitulate the arguments adduced by Becquerel, myself, and Heintz, against the opinion of Bird, who maintains that this sediment is always urate of ammonia, as the actual nature of the deposit has been so completely established. I will here only remark that, as I long ago found, and as Liebig has since confirmed, scarcely any ammonia occurs in urine, and that, according to the direct analysis of the sediment made by Heintz, scarcely 1% of ammonia could be found in it.

Much has also been written to prove that uric acid does not exist free in the urine, but in a state of combination with alkalies; but it requires only a moderate knowledge of the properties of uric acid and its salts to perceive that there is nothing wonderful in the presence of an acid urate in an acid fluid, and that the occurrence of acid urate of soda is perfectly natural. Ure* and Lipowitz† were the first to direct attention to the circumstance which was afterwards very prominently brought forward by Liebig, that phosphate of soda might be one of the solvents of uric acid, and that thus an acid urate of soda and an acid phosphate of soda might be produced. Berzelius‡, however, has remarked that there are very few solutions of alkaline salts in which uric acid does not dissolve more readily than in water, and that it, for the most part, separates from these solutions as uric acid, and not as an acid alkali-salt. I have, however, especially remarked (Op. cit.) that uric acid may extract soda from alkaline lactates, and from compounds of the alkalies with other organic acids, and that the acid salt thus formed communicates an acid reaction to the previously neutral fluid; the urate of soda then separates from a pure mixture in a crystalline form, but from a solution containing extractive matter, as the urine, in an amorphous state, and dissolves again very readily when heated to 50°.

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* Séméiotique des Urines, pp. 51 and 249, or pp. 40-50 and 126-180 of the German Translation.

† Jahresber. d. phys. Ch. 1844. S. 26.

‡ Müller's Arch. 1845. S. 230-261.

The appearance of this sediment of urate of soda (Prout's amorphous and impalpable yellow sediment) is by no means to be regarded as a pathological symptom; it is nothing more than an augmentation of a salt normally existing in the urine, induced by simple physiological relations. Hence we especially observe the formation of such sediments, when, for any reason, the due interchange of the gases in the lungs does not take place, or when, from disturbances of the circulation, the blood does not readily permeate the pulmonary vessels. Thus a sediment of this nature may be noticed in men and animals when there is an insufficiency of proper exercise; carnivorous animals, which in their natural state secrete so little uric acid, after long confinement frequently pass a sedimentary urine, especially when they have been reared in cages, and have been attacked by osteomalacia. In fully developed emphysema, or even when only a part of the lung has lost some of its elasticity, a sedimentary urine is one of the most common symptoms. Heart-diseases, enlargements of the liver, &c., are associated with disturbances of the circulation, and hence give rise to a sedimentary urine. It is to such diseases as these that illogical, ontological names—such as hæmorrhoids, gout, &c.—

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[*] Medical Gazette, vol. 35, p. 188.

[†] Ann. d. Ch. u. Pharm. Bd. 38, S. 350.

[‡] Jahresber. Bd. 26, S. 873.

have been applied. Large masses of secreted urate of soda are found in no disease, except in the true granular liver, which obviously can never exist without considerable disturbance of the circulation. In fever also, the due relation between respiration and circulation is no longer maintained, and hence there is an augmentation of the uric acid in the urine; for none but mere chemists could be led to the erroneous idea, that in fever too much oxygen is conveyed to the blood—in short that fever is attended by too rapid a process of oxidation. Becquerel's extended observations on urine in diseases, may be profitably compared with the above results of my own experience.

Bird[*] and many others maintain that in gout there is an increased secretion of uric acid; my own experience, however, perfectly confirms that of Garrod,[†] who found that there was a constant and well-marked diminution of the uric acid in the urine before the paroxysm in acute gout, and always in chronic gout, (a term which applies only to those cases in which the disease is accompanied by depositions in the joints;) while, on the other hand, in rheumatism, especially in acute articular rheumatism, the amount of uric acid in the urine is very much increased—a point in which all observers coincide.

It is extremely seldom that *free uric acid* is found in freshly discharged urine, and its presence there may generally be regarded as a sign of some extremely severe morbid process.

I have *never* been able to find separated crystals of uric acid in urine immediately after its emission, although they may often be found when it has stood for an hour or more. In the great majority of cases the uric acid is formed from the urate of soda after the exposure of the urine to the atmosphere, by the process of acid urinary fermentation which has been so carefully studied by J. Scherer.[‡]

Healthy and febrile urine only differ in this point, that the one contains additional elements by which the formation of lactic acid is excited and promoted. We shall return on a future occasion to this beautiful investigation of Scherer's. I have never seen free uric acid discharged directly from the bladder with the urine except in cases of the calculous diathesis or of pre-existing gravel.

Even in alkaline urine it is very seldom that *urate of ammonia* occurs as a sediment; in these cases it is found in white opaque granules, which, as has been already stated, when seen under the microscope, appear as dark globules, studded with a few acicular crystals. It scarcely ever occurs except in urine which, by long exposure to the air, has undergone the alkaline fermentation. Even in the alkaline urine of patients with paralysis of the bladder dependent on spinal disease, it is very rarely that I have found these clusters of urate of ammonia. In the alkaline urine that is sometimes passed in other conditions of the system, it is never found.

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[*] Urinary Deposits, 3rd. edit., p. 134.

[†] Medico-Chir. Trans. Vol. 31, p. 86.

[‡] Untersuch. S. 1-17.

Uric acid, like urea, also exists in the *blood;* it has been found there in healthy as well as in diseased states, and especially after extirpation of the kidneys by Strahl and Lieberkühn,* as well as recently by Garrod,† who observes that in arthritis (but not in acute articular rheumatism,) it is invariably, and in Bright's disease it is very often, increased in the blood.

My own observations for the most part confirm those of Garrod. I first happened to convince myself of the presence of uric acid in the blood of carnivora in examining the blood of a very large mastiff who died in consequence of an artificial gastric fistula which I had established. The serum was freed from its albumen by boiling and with the aid of acetic acid; the strongly evaporated filtered fluid was extracted with alcohol in order that urea might be sought for; the residue, insoluble in alcohol, exhibited, under the microscope, most unquestionable crystals of uric acid; my attention being thus drawn to the subject, I examined the blood of two other dogs by the same mode of analysis, and convinced myself of the presence of uric acid, not only by the microscope, but also by the murexide test. Garrod asserts that he has often found uric acid in the blood of healthy men, while Strahl and Lieberkühn failed equally in detecting it in the blood of men and of birds; once only they found uric acid in the blood of a dog; they recognised it however with great distinctness, and on many occasions, in the blood of frogs, dogs, and cats, after the extirpation of the kidneys. Garrod found 0·005%, 0·004%, and, in one case, even 0·0175% of uric acid in the serum of the blood of gouty patients. In acute articular rheumatism he could only discover traces of uric acid in the blood; in Bright's disease the uric acid of the blood occurred in very variable quantities; (from 100 parts of serum he obtained the following quantities, 0·0037, 0·0055, 0·0012, and 0·0027 parts.)

In Germany we have few opportunities of repeating Garrod's experiments regarding the quantity of uric acid in the blood of gouty patients, for in this country we should certainly hesitate before abstracting such masses of blood as he employed in his analyses; he never operated on less than two pounds of blood.

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* Harnsaure im Blut, u. s. w. Berlin. 1848.

† Medico-Chir. Trans. Vol. 31, pp. 87-92.

Urate of soda is very often found in gouty nodules or concretions, as is shown by the analyses of Wollaston, Laugier, Wurzer, Pauquy, and Bor. My own limited observations entirely accord with the statements of these chemists. The concretions form, for the most part, yellowish white, soft masses, speckled here and there with red spots; on exposure to the atmosphere they harden; examined under the microscope they present the most beautiful tufts of crystals of urate of soda.

Wolf* asserts that he has discovered uric acid in the sweat of arthritic patients; I have made many attempts to detect it in such cases, but have never yet been successful.

Unfortunately the idea of *gout* in medicine is so vague that it would be well, if, for the present, it were altogether expelled from science. The pathologists are wont to refer to the chemist for the elucidation of this singular disease, but they should rather consider that it is their place to furnish the chemist with more exact ideas regarding this mysterious affection before seeking for an explanation. It must, moreover, be observed that, notwithstanding their assertions to the contrary, pathologists have not yet taught us to distinguish any appreciable difference between gout and rheumatism; while we find from pathological anatomy that the group of symptoms which has generally been regarded as characteristic of the former of these diseases may yield very different results in reference to alterations in the tissues as revealed after death. We most commonly meet with diseases of the osseous system, with osteomalacia in young persons and adults, an affection in which the bones become poorer in earths, and consequently more flexible, than in their natural state, or with osteoporosis or osteospathyrosis, where there is resorption of the cartilage as well as of the earths, as resulting from gout: but the essential principle of the disease cannot lie in this resorption, since often in one and the same bone we find sclerosis and porosis; the change which the bone undergoes is solely dependent on the nature of the exudation which is thrown out; if the latter be very consistent (fibrinous?) it puts on an appearance of callus, deposits an excess of bone-earth, and the affected part becomes sclerotic; if, on the other hand, it be fluid, resorption takes place, and the result is osteoporosis; if it exhibit a tendency to decomposition and become ichorous, caries as well as pyæmia may ensue. Unfortunately, however, these alterations in the osseous system are not peculiar to gout, but occur both from purely local causes, and from other general diseases, especially from syphilis. The diseased condition of the osseous system, however constantly it may be observed in gout, when we adhere to the strictest definition of the term, affords us no firm starting-point; we must, consequently, have recourse to the nodules and concretions, but these earthy deposits may exist independently of gout, and there remains no characteristic of the nature of gout excepting the concretions of urate of soda; yet how seldom do even these occur; and how far advanced must be the malady before we can base our diagnosis on their presence! The accumulation of great quantities of uric acid in the blood, independently of other symptoms, is also devoid of importance, since, according to Garrod, this may likewise occur in Bright's disease. In a word, we know not the nature of arthritis; and if this ever be elucidated by physiologico-chemical investigations, I believe that the sole method which will conduce to this end will be that of ascertaining the relation in which the chemical constitution of the blood and urine stands to the above-named diseases of the osseous system, and to osteomalacia in particular.

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* Diss. sist. casum Calculositatis. Tub. 1817.

It seems to us still more inappropriate and still less in accordance with a rational natural inquiry, if, basing our views on a preconceived and misunderstood proposition, we philosophise on the analogy of "gout, gravel, and stone"; *à priori* explanations of morbid processes such as have been attempted in the organico-chemical department of medicine, have usually failed in yielding any results, from the misconception that, without physiology and pathological anatomy, medicine might be established in accordance with subjective chemical views. The pretended oxidation of the constituents of the blood, which was supposed to explain phthisis as well as gout and stone, is not the simple method by which alone specific diseases or individual well-characterised processes can be explained with scientific accuracy. For *there are no acute and but few chronic diseases in which the oxidation of the constituents of the blood is not diminished or impeded.* The proof of the assertion will, in a future part of this work, be made as evident as the fact *that there is no disease characterised by a too sudden or rapid oxidato n of the blood.*

Origin.—Since we have already (see p. 168) mentioned that urea is in part derived from uric acid, there can be no doubt that the latter, like the former, must rank amongst the excrementitious matters. Although we have no numerical proof that in human urine the urea stands in an inverse ratio to the uric acid, that is to say, that with an augmentation of the uric acid there is a corresponding diminution of the urea, yet the numerical results of Becquerel and others show that there is at least such an approximate ratio. The recent experiments of Wöhler and Frerichs,* in which the introduction of uric acid into the organism by the *primæ viæ* or by the veins, was followed by an augmentation of the urea and oxalate of lime in the urine, afford tolerably strong evidence that the uric acid in the animal organism undergoes a decomposition into urea and oxalic acid precisely similar to that which can be artificially induced by peroxide of lead. Now, if the urea be produced from the uric acid by the partial oxidation of the latter, anything impeding this process must cause less urea and more uric acid to be separated by the kidneys, and hence we see why the amount of uric acid in the urine must be increased in fevers and other disturbances in the circulation and respiration; we have seen that in like states oxalate of lime and lactic acid increase for a precisely similar reason, and without wishing to introduce rude chemical views into the science of general life, nothing seems more simple, and in accordance with nature, than this explanation of the origin and augmentation of uric acid. We regard uric acid as a substance which stands one degree higher in the scale of the descending metamorphosis of matter than urea. The present condition of science does not admit of our specially indicating the substances from which it is first produced, or the locality in which it is formed.

Sediments of urate of soda are commonly ranked amongst the critical discharges. A rational system of medicine can no longer, in accordance with the doctrines of Hippocrates, regard these excretions as true crises of diseases, but must rather consider them only as incidental symptoms, or as necessary consequences of certain processes. In the present day we regard the crises merely as very abundant eliminations of excrementitious matters which must occur when the substances rendered effete during the fever, and which have accumulated in the blood while the functions of the excreting organs were more or less impeded, are fit for simultaneous secretion, and are thus given off to the outer world by their ordinary channels.

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* Ann. d. Ch. u. Pharm. Bd. 65, S. 338-342.

Inosic Acid.—$C_{10}H_6N_2O_{10}.HO$.

Chemical Relations.

Properties.—This acid is not crystallisable; it forms a syrupy fluid, which is converted by alcohol into a solid, hard mass; it dissolves readily in water, but is insoluble in alcohol and ether; it reddens litmus strongly, possesses an agreeable taste of the juice of meat, is decomposed by heating, and in part, if its solution be boiled.

Composition.—According to the above formula, which Liebig,* the discoverer of this acid, deduced from his analysis of the baryta-salt, this acid consists of:

Carbon	10 atoms	32·787
Hydrogen	6 „	3·279
Nitrogen	2 „	15·300
Oxygen	10 „	43·716
Water	1 „	4·918
		100·000

The atomic weight of the hypothetical anhydrous acid=2175·0, and its saturating capacity=4·597. This acid is unquestionably no simple oxide of a ternary radical, but contains certain proximate constituents; its products of metamorphosis have, however, as yet been so little studied that we cannot even form any conjecture regarding the adjunct or the peculiar acid contained in it. Liebig remarks that it may be regarded as composed of 1 equivalent of acetic acid, 2 equivalents of oxalic acid, and 1 equivalent of urea.

Combinations.—The alkaline inosates are soluble in water, are crystallisable, and, when heated on a platinum spatula, diffuse a powerful and agreeable odour of roasted meat.

Inosate of potash, $KO.C_{10}H_6N_2O_{10}+7HO$, occurs in long, delicate, four-sided prisms; on the addition of alcohol to a concentrated aqueous solution, this salt separates in fine nacreous scales.

Inosate of baryta, $BaO.C_{10}H_6N_2O_{10}+7HO$, crystallises in long four-sided scales of a nacreous lustre, which, when dry, have the aspect of polished silver; it effloresces readily, dissolves freely in hot, very slightly in cold water, and not at all in alcohol. If a solution, saturated at 70,° be heated to boiling, a part of the salt is deposited in the form of a resinous mass.

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* Ann. d. Ch. u. Pharm. Bd. 62, S. 325-335.

Inosate of copper forms a light blue, amorphous powder, insoluble even in acetic acid.

Inosate of silver is amorphous, white, and slightly soluble in pure water.

Preparation.—If the mother-liquid of the juice of flesh, after the creatine has crystallised and been removed, (see p. 136,) be gradually treated with alcohol till the whole become milky, it deposits, in the course of a few days, yellow or white granular, foliated, or acicular crystals of the inosates of potash and baryta, mixed with creatine. Chloride of barium must be added to the hot aqueous solution of these crystals; on cooling there is a deposition of crystals of inosate of baryta, which, by recrystallisation, are rendered perfectly pure. By decomposing this salt with sulphuric acid, or the copper-salt with sulphuretted hydrogen, the acid is obtained in a state of purity.

Tests.—So little is yet known regarding the properties of this acid, that the only test we can rely upon is the ultimate analysis.

Physiological Relations.

Liebig has hitherto only found this acid in the fluid of flesh. The few facts which we at present possess regarding this acid throw no light on its mode of formation. From the great quantity of oxygen which it contains, it must be regarded as a product of the decomposition of effete tissues.

GLYCOCHOLIC ACID.—$C_{52}H_{42}NO_{11}.HO$.

Chemical Relations.

Properties.—This acid, which has been named, *par excellence, bilic* or *cholic acid*, forms extremely delicate needles, which remain unchanged at 136°; it has a bitterish-sweet taste, dissolves in 120·5 parts of hot, and 303 parts of cold water; is readily soluble in spirit, but only slightly in ether; it does not crystallise on evaporating the alcoholic solution, but separates as a resinous mass; but it crystallises from the spirituous solution, mixed with water and exposed in the air to gradual evaporation. The aqueous solution of this acid reddens litmus strongly. It dissolves without change in concentrated acetic acid, cold sulphuric acid, and hydrochloric acid.

The aqueous solution of this acid is not precipitated by acids, neutral acetate of lead, corrosive sublimate, or nitrate of silver;

in alkalies it dissolves freely, being precipitated from them by acids, in a resinous form; on standing, especially after the addition of a little ether, the resinous precipitate becomes crystalline. A solution of the acid in combination with an alkali yields no precipitate with chloride of barium; but there are precipitates on the addition of the salts of the oxides of lead and copper and peroxide of iron; nitrate of silver, when added to very dilute solutions, yields a gelatinous precipitate, which, on warming, again dissolves, and on cooling gradually assumes a crystalline form. By prolonged boiling with a solution of potash, or still better, with baryta-water, this acid becomes resolved into the non-nitrogenous cholic acid and glycine (see p. 152). When boiled with concentrated sulphuric or hydrochloric acid, it is resolved into choloidic acid and glycine. (Strecker.[*])

With sulphuric acid, and either sugar or acetic acid, glycocholic acid yields the same reaction as cholic acid (see p. 123.)

If glycocholic acid be submitted to prolonged ebullition in water, it becomes perfectly insoluble, and breaks up into fragments of six-sided tablets. To this modification the name of *paracholic acid* has been applied by Strecker.

Composition.—From numerous analyses of glycocholic acid and its salts, Strecker[†] has deduced for it the above formula, according to which it consists of:

Carbon	52	atoms	67·097
Hydrogen	42	,,	9·032
Nitrogen	1	,,	3.011
Oxygen	11	,,	18·925
Water	1	,,	1·935
			100·000

The atomic weight of the hypothetical anhydrous acid = 5700; and its saturating capacity = 1·754.

Hardly a doubt can remain that this is a conjugated acid, when we consider, on the one hand, that we are acquainted with another acid (hippuric acid) from which the same nitrogenous body, glycine, may be separated by acids, and that, on the other hand, there is another acid from which the same non-nitrogenous acid, cholic acid, is liberated by acids, another body, taurine, being simultaneously produced; (this taurine in the taurocholic acid taking the place of the glycine in the glycocholic acid.) In glycocholic acid we cannot, however, consider glycine, as we know it in its isolated state, to be the adjunct of cholic acid, but must rather assume that the true adjunct of cholic acid, as in the case of hippuric acid, undergoes a change during its separation, by which it forms the body known to us as glycine. If, as in hippuric acid, we regard this adjunct as a group of atoms isomeric with fumaramide, the rational formula of glycocholic acid will be= $C_4H_3NO_2.C_{48}H_{39}O_9.HO$.

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[*] Ann. d. Ch. u. Pharm. Bd. 66, S. 1-43.

[†] Ibid. Bd. 65, S. 1-37.

Combinations.—With alkalies and alkaline earths, glycocholic acid forms very soluble salts; its compounds with the oxides of the heavy metals are, however, insoluble; the glycocholate of silver alone being soluble in boiling water.

Glycocholate of soda, $NaO.C_{52}H_{42}NO_{11}$, separates from its alcoholic solution, on the addition of ether, in large, glistening, white clusters of radiating needles, resembling wavellite; it is not crystallisable from its watery or spirituous solutions; it dissolves very readily both in water and in spirit (1 part dissolving in 2·56 of spirit at 15°); when heated it melts, burns with a smoky flame, and leaves an ash containing cyanides. *Glycocholate of potash* behaves in a similar manner.

Glycocholate of ammonia, $H_4NO.C_{52}H_{42}NO_{11}$, occurs in crystals precisely similar to those of the soda-salt, when it is gradually separated from an alcoholic solution by ether; it dissolves readily in water, yields ammonia on boiling, and then has a faintly acid reaction.

Glycocholate of baryta, $BaO.\ C_{52}H_{42}NO_{11}$, is amorphous, has a strongly sweet and slightly bitter taste, is soluble in water and in alcohol, and is not decomposed by carbonic acid.

Preparation.—This acid occurs in the bile of most animals, but it is best prepared from the bile of the ox by one of the two following methods.—The bile first carefully dried in the water-bath, and subsequently *in vacuo,* must be extracted with cold absolute alcohol, and ether must be gradually added to the filtered solution, which is thus rendered turbid, and soon deposits a brownish, tough, resinous mass. If the fluid be now only slightly coloured, we must decant it from the semi-fluid precipitate into another vessel, and again gradually add ether; the fluid again becomes milky, and deposits more resinous matter; after a time, however, glistening star-like tufts of crystals are deposited, which must be washed with alcohol to which a tenth part of ether has been added, and then rapidly placed *in vacuo,* because the crystals, when moist with ether, rapidly deliquesce into a varnish-like mass; after drying they cease to be acted on by the atmosphere. These crystals are a mixture of the glycocholates of potash and soda. On precipitating the aqueous solution of these crystals with acetate of lead, decomposing the precipitate with carbonate of soda, evaporating the solution of glycocholate of soda, re-dissolving in alcohol, and again (in the same manner as before) crystallising by means of ether, we obtain a tolerably pure glycocholate of soda, which, when dissolved in water and treated with dilute sulphuric acid, after a time deposits crystals mingled with oily globules. The latter may be removed by washing with water, leaving the glycocholic acid in a state of purity.

The following is a shorter method of obtaining this acid. The yellowish precipitate thrown down by sugar of lead from fresh bile must be extracted with boiling spirit of 85% and sulphuretted hydrogen passed through the solution. If water be added to the filtered fluid and the mixture be allowed to stand for a considerable time, the acid will separate in a crystalline form; in this case, however, it is better to decompose the lead-salt by carbonate of soda, and then to proceed in accordance with the former method.

Crystallised bile, which is a mixture of the glycocholates of potash and soda, was first prepared by Platner.*

Tests.—In attempting to determine the amount of bile in an animal fluid, it is always necessary that the albuminous matters, the substances soluble in water only, and the fats, should be as completely as possible separated. We consequently, in the first place, obtain an alcoholic extract of the substance to be investigated, and ascertain by Pettenkofer's test whether any derivative of the bile be present in it. This point being decided, we can only determine whether one of the acids contained in fresh bile—glycocholic or taurocholic acid, or one of their derivatives, cholic or choloidic acid—be present, when we have a considerable amount of matter to work upon. To pursue this inquiry, we must gradually add from 8 to 12 times its volume of ether to the extract obtained by strong alcohol, and allow the mixture to stand for from 24 to 48 hours; by this time the turbidity of the fluid will have disappeared, and a sediment will have formed, which is either flocculent and viscid, so as to adhere to the walls of the vessel, (in which case it consists for the most part of albuminous or extractive matter,) or is a resinous, semi-fluid, tough mass (alkaline taurocholates or choloidates), or consists of tufts of well-formed crystals of various sizes, visible to the naked eye, and composed either of cholate or glycocholate of soda. It is worthy of remark that even the smallest quantities of the alkaline glycocholates crystallise from their solution in this way. (From a solution of about 0·07 of a gramme of glycocholate of soda in 150 parts of alcohol, I obtained most beautiful crystals of the salt on the addition of 560 grammes of ether.) These crystals must, however, always be examined microscopically, or at all events with a lens, as many other salts (acetate of soda for instance) separate in a crystalline form under this mode of treatment: they form six-sided prisms with a single very oblique plane of truncation, and as their aqeous solution reacts with Pettenkofer's bile-test, no doubt can remain regarding the presence of glycocholic acid. If the crystals be obtained either in a state of purity or surrounded by syrupy matter, we must separate the acid from the alkali by a little sulphuric acid, and extract with ether, in which the conjugated cholic acids as well as choloidic acid are almost insoluble; if the crystallisable cholic or glycocholic acid be thus isolated, we can determine regarding the presence or absence of one or other of them by boiling with a solution of potash, when, if glycocholic acid be present, ammonia is developed; moreover, the cholate of baryta is a crystallisable salt, while the glycocholate of baryta is amorphous. Glycocholate acid resembles choloidic acid in being only slightly soluble in ether; they may, however, generally be distinguished by the crystallisability of the former acid and of its salts from ethereo-alcoholic solutions; the glycocholate of baryta, indeed, resembles the choloidate in being uncrystallisable, but it differs from the latter in being soluble in water. We shall point out the means of distinguishing between glycocholic and taurocholic acids in our observations on the latter acid.

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* Ann. d. Ch. u. Pharm. Bd. 51, S. 105; Journ. f. pr. Ch. Bd. 40, S. 129-133.

Physiological Relations.

Occurrence.—As far as our investigations have hitherto extended, this acid has been found in the *bile* of all animals, with the exception of the pig. In reference to its occurrence in other parts and fluids of the animal body, we have only to repeat what has already been said in pp. 124-5 regarding cholic acid. We meet with such minute quantities of biliary matter in the intestinal canal, in the blood, and in exudations, that until recently they have been, for the most part, entirely overlooked, and it is only by means of Pettenkofer's admirable test that we can now detect them. Important as it would be in a physiological point of view to ascertain whether cholic acid or the conjugated biliary acids occur in the blood, and whether these or choloidic acid occur in the intestine, we must for the present leave these questions altogether undecided.

Kunde, one of my pupils, has very distinctly recognised the presence of biliary matters by means of Pettenkofer's test in the fluid from the hydrocele of an otherwise healthy man. By the same test he was able to demonstrate the presence of biliary matters in the blood of frogs, whose livers he had extirpated. (Of six frogs on which he operated, only two survived.)

Origin.—We have already (see p. 126) attempted to show the probability that cholic acid obtains its essential elements from the fats, and that, in short, it is oleic acid conjugated with a non-nitrogenous body. But in glycocholic acid we again meet with the same nitrogenous adjunct which we have already encountered in hippuric acid, and which, consequently, seems to be an ordinary product of decomposition of nitrogenous bodies. We have already remarked (see p. 197) that we are not in ac ondition to name the proximate source of this adjunct, which is, however, isomeric with fumaramide.

This is not the most appropriate place for entering into the physiological reasons for showing the part which the fat takes in the formation of the principal constituents of the bile, or for balancing the reasons for or against the formation of bile within the hepatic cells. These are subjects pertaining to the second department of our work, in which we shall consider the bile in general as an animal secretion. We may, however, be permitted to remark that the possibility of the primary formation of this acid in the blood is indicated partly by the above-mentioned experiments of Kunde, and partly by the not unfrequent occurrence of icterus independently of any hepatic affection (Virchow), that is to say, without infiltration of the parenchyma of the liver and of the hepatic cells with bile-pigment.

Uses.—As we are not at present accurately acquainted with the changes which glycocholic acid undergoes in the intestinal canal, we are unable to state whether this acid exerts any special action in the process of digestion.

Hyocholic Acid.—$C_{54}H_{43}NO_{10}.HO$.

Chemical Relations.

Properties.—This acid, discovered and accurately examined by Gundelach and Strecker*, forms a white resinous mass, which melts in water at 100° and, like choloidic acid, may be drawn out in long threads; when perfectly dry it does not melt at a temperature under 120°; it is only slightly soluble in water, dissolves readily in alcohol, and not at all in ether; it reddens litmus. It dissolves unchanged in cold concentrated nitric and sulphuric acids; but when boiled for some time in either of those acids it yields, like glycocholic acid, glycine and a resinous acid similar to choloidic acid; with concentrated sulphuric acid and either sugar or acetic acid, it yields, like the other biliary acids, a purplish-violet solution; it is only decomposed by a solution of caustic potash, when the mixture is so concentrated as to solidify on cooling. It is unchanged by digestion in moderately concentrated sulphuric acid and peroxide of lead; putrefaction of the bile seems to exert no influence on it; when treated with fuming nitric acid, or decomposed by chromic acid, it yields the same products as choloidic acid, namely *cholesteric acid*, butyric acid, caproic acid, &c.

Composition.—According to Gundelach and Strecker, this acid may be obtained in an anhydrous state, so as in its combination with bases to lose no water. From their analyses of the free acid, as well as of its salts, these chemists have deduced the above formula, in accordance with which the free anhydrous acid consists of:

Carbon	.... 54 atoms	.... 70·28
Hydrogen	.... 43 „	.... 9·33
Nitrogen....	.... 1 „	.... 3·04
Oxygen	.... 10 „	.... 17·35
		100·00

The atomic weight=5762·5, and its saturating capacity=1·735.

This acid contains 2 atoms of carbon and 1 atom of hydrogen more, but 1 atom of oxygen less, than glycocholic acid; the fact that, when treated with concentrated mineral acids, it likewise yields glycine, tends to confirm the hypothesis, that hyocholic acid also contains the glycine-yielding adjunct isomeric with fumaramide, and that so much plus of carbon and hydrogen, and minus of oxygen, are respectively added to, and deducted from the non-nitrogenous acid, that the rational formula for this acid would be$=C_4H_3NO_2.C_{50}H_{40}O_8$. But as hyocholic acid when decomposed with nitric acid yields the same volatile fatty acids and cholesteric acid, the non-nitrogenous acid, contained in hyocholic acid, may be presumed to have a constitution analogous to cholic acid (see p. 126), and besides the group of atoms $C_{12}H_6O_6$ which yields the cholesteric acid ($C_8H_4O_4$) to contain another fluid fatty acid of the formula $C_nH_{n-3}O_3$ in place of the oleic acid in the cholic acid; and this in point of fact admits of being calculated by subtracting the group of atoms $C_{12}H_8O_8$ from the hydrate of the non-nitrogenous hyocholoidic acid; $C_{50}H_{41}O_9-C_{12}H_6O_6=C_{38}H_{35}O_3$, which is exactly the formula of doeglic acid (see p. 116).

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* Ann. d. Ch. u. Pharm. Bd. 62, S. 205-232.

That this calculation is a mere fiction is sufficiently obvious, but we believe that such fictions should not be altogether unnoticed, since they stimulate us to further enquiry, even if it were only to determine whether an acid isomeric or identical with doeglic acid existed in the fat of the pig.

Combinations.—The *alkaline hyocholates* are not crystallisable; they are soluble in water and alcohol, but not in ether, which completely precipitates them from their alcoholic solutions. Their taste is bitter without any sweet after-taste, and they redden litmus; like soaps, they are precipitated from their aqueous solutions by alkaline salts, the precipitate containing the base of the salting added in excess; they melt and are inflammable when heated; with the *salts of baryta, lime, and magnesia*, they yield white precipitates soluble when the mixture is raised to the boiling temperature. Their aqueous solutions are precipitated by most of the metallic salts, but their alcoholic solutions are not affected by these reagents. On the addition of an acid to the aqueous solution, the hyocholic acid is entirely precipitated. Neutral acetate of lead yields a white precipitate which does not cake on boiling.

Hyocholate of potash, $KO.C_{54}H_{43}NO_{10}$, is in its moist state a white amorphous mass which melts in the water-bath, and dissolves as long as it contains either water or spirit. It does not dry at a temperature under 120°.

Hyocholate of soda, $NaO.C_{54}H_{43}NO_{10}$, forms when dry a brownish mass, which when finely triturated, becomes of a snow-white colour; it has a persistent bitter taste without any sweet after-taste. Its solutions are neutral, and are not rendered turbid by carbonic acid. It is precipitated from its alcoholic solution by ether, and from its aqueous solution by soda-salts; it melts when heated, dissolves, and burns with a bright but smoky flame.

Hyocholate of ammonia, $H_4NO.C_{54}H_{43}NO_{10}$, is a white crystalline powder. Its solutions become turbid on boiling, and assume an acid reaction. It may be dried over sulphuric acid without loss of ammonia.

Hyocholate of baryta, $BaO.C_{54}H_{43}NO_{10}$, is a gelatinous substance, freely soluble in spirit, moderately soluble in hot water, and slightly so in cold water.

Hyocholate of lime, $CaO.C_{54}H_{43}NO_{10}$, is white, amorphous, and rather more soluble in water than the baryta-salt; it is precipitated from its spirituous solution by water and by carbonic acid.

Hyocholate of lead is a white powder, which neither cakes when boiled with water nor when dried; it is slightly soluble in water, but freely in spirit, from which it (like all the other salts of this acid) is precipitated by ether. Red litmus is turned blue by the alcoholic solution.

Hyocholate of silver, $AgO.C_{54}H_{43}NO_{10}$, occurs as a gelatinous precipitate, which, on boiling, becomes flocculent; it dissolves freely in spirit, slightly in cold, but somewhat more easily in hot water.

Preparation.—The precipitate caused by the addition of a solution of sulphate of soda to fresh swine's bile is dissolved in absolute alcohol, decolorised by a little animal charcoal, and the soda-salt of the acid precipitated by ether from the alcoholic solution; this is decomposed by dilute sulphuric acid, and the precipitate is dissolved in alcohol, from which the hyocholic acid is thrown down by the addition of water.

Tests.—It is only with glycocholic and choloidic acids that this acid can possibly be confounded. From the former it may easily be distinguished by the circumstance that neither it nor its salts can be obtained in a crystalline state by the addition of ether to alcoholic solutions. It is, however, not so readily distinguishable from the latter, because, without an elementary analysis, it is impossible to determine its nitrogen; and because, further, when treated with concentrated hydrochloric acid it yields too little glycine to be recognised with certainty, unless, indeed, we have a very large supply of the material to be investigated. The fact that hyocholate of lead neither cakes when dried nor when boiled with water, while the opposite is singularly the case with the glycocholate, affords a tolerably characteristic test. Other differences are for the most part only gradual, and are inapplicable as tests to enable us to distinguish between small quantities of these acids.

Physiological Relations.

This acid has hitherto only been found in the *bile of the pig*, where it exists in combination with soda, potash, and a little ammonia. Our remarks on the origin and uses of glycocholic acid are equally applicable to hyocholic acid.

TAUROCHOLIC ACID.

Chemical Relations.

Properties.—This acid, which has also been named *choleic acid*, and was formerly known as *bilin*, has not yet been obtained in a state of perfect purity, that is to say, free from glycocholic acid; it cannot be obtained in a crystalline state, and it is more soluble in water than glycocholic acid, while its acid properties are far weaker. It dissolves fats, fatty acids, and cholesterin in large quantities, and is thus the cause why glycocholic acid is not precipitated from fresh ox-bile by acetic or the mineral acids. On exposure to the air, as well as on evaporating a solution of the free acid, decomposition ensues. When boiled with mineral acids it becomes resolved into taurine and choloidic acid; when boiled with alkalies, into taurine, and cholic acid; and when treated with sulphuric acid and sugar, it gives the same reaction as the other essential acids of the bile. The characters of its salts are, however, very distinct from those of the other biliary acids.

Composition.—As this acid, like glycocholic acid, becomes resolved, when acted on by mineral acids and by alkalies, into choloidic or cholic acid, while in place of glycine it yields taurine, Strecker,* to whom we are especially indebted for our knowledge of this acid and of its properties, correctly argues that its composition is perfectly analogous with that of glycocholic acid, the only difference being that the adjunct in this case is taurine. Abstracting from the formula for taurine 1 atom of water, he assumes that the empirical formula of this acid $=C_{52}H_{45}NS_2O_{14}$, and the rational formula $=C_4H_6NS_2O_5.C_{48}H_{39}O_9$. We must therefore regard taurocholic acid as containing an adjunct rich in sulphur, which, on its separation from the cholic acid, becomes converted into taurine, whose properties we have already described at p. 179. By elementary analyses of a mixture of pure alkaline glycocholates and taurocholates, obtained directly from fresh bile, Strecker has further confirmed his view regarding the composition of this acid. Pure taurocholic acid must, therefore, contain 6·213$\frac{0}{0}$ of sulphur, while its atomic weight must=6437·5 and its saturating capacity be 1·553.

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* Ann. d. Ch. u. Pharm. Bd. 66, S. 43-61.

Combinations.—The *alkaline taurocholates* dissolve readily in water and in alcohol, but are perfectly insoluble in ether; they have no reaction on vegetable colours, and attract water from the atmosphere, but do not deliquesce; when kept for a long time in contact with ether they crystallise; their aqueous solutions have a sweet taste with a bitter after-taste, and do not decompose when evaporated, or when exposed to the air, provided they be pure. These salts when heated melt and burn with a bright smoky flame. Carbonic acid does not decompose their alcoholic solution; their aqueous solution is not precipitated by acids, nor by the alkaline sulphates or chlorides (like the alkaline hyocholates), but by concentrated alkaline solutions; it is not precipitated by the salts of baryta, lime, or magnesia, even on the addition of ammonia, or by neutral acetate of lead; but on the addition of basic acetate of lead, there is a plastery precipitate which dissolves in boiling water, and even more freely in boiling alcohol, and is also soluble in an excess of acetate of lead. Nitrate of silver, even after the addition of ammonia, does not precipitate the taurocholates, neither does corrosive sublimate, but precipitates are induced by nitrate of suboxide of silver, and protochloride of tin. Nitrogenous substances, mucus for instance, set up a process of decomposition in solutions of the alkaline taurocholates, which may be readily ascertained by the circumstance that the solutions then become precipitable by dilute acids. The products which are formed are taurine, alkaline cholates or choloidates, and probably certain combinations of these substances with taurocholic acid that has escaped decomposition. In aqueous solutions of pure alkaline taurocholates, these decompositions are not observed to occur.

Preparation.—We have already remarked, that this acid has never yet been prepared in a state of complete purity. In order to separate it as thoroughly as possible from the glycocholic acid which always accompanies it, we in the first place remove from the purified ox-bile the greater part of the glycocholic acid and of the fatty acids by means of neutral acetate of lead, and then precipitate by basic acetate of lead, to which we may add a little ammonia. This precipitate must be decomposed with carbonate of soda, and we must extract the solid residue of the filtered fluid with alcohol. On the addition of ether to the alcoholic solution, a tolerably pure taurocholate of soda is immediately precipitated in the form of a resinous, semifluid, yellow mass. If this be dissolved in a small quantity of water, and all that is precipitable by acetate of silver be thrown down, and if the fluid after filtration be precipitated with basic acetate of lead, and the precipitate, after being thoroughly diffused in a little water, be treated with sulphuretted hydrogen, we obtain tolerably pure taurocholic acid after evaporating *in vacuo*.

Tests.—No great weight can be attached to any of the differences in the reaction of the salts of glycocholic and taurocholic acids, when the quantity of the substance presented to us for examination is very small. If, however, we have sufficient material, we must obtain the acids from the alcoholic extract with precisely the same precautions as we have indicated in the preceding pages in reference to each of these acids; from the ratio of the precipitate caused by the sugar of lead to that caused by the acetate of lead, we must draw our conclusions regarding the relative quantities of the two acids, and then, by treating the alcoholic solution of the soda-salt with ether, we can determine this point with certainty; indeed, we shall always be most decisively convinced of the presence of taurocholic acid by the exhibition of the taurine, which, even if obtained in only very small quantities, may be recognised with certainty by crystallometric examination under the microscope. Unfortunately, however, the quantities of taurine are so minute, unless when we are acting directly on bile, that it cannot be distinguished and recognised with certainty either by the above means or by its relation towards nitrate of silver and other metallic salts. Nothing further remains for us but to determine the presence of sulphur; having ascertained by Pettenkofer's test that biliary matter is present in the substance under examination, we must extract the spirituous extract with cold absolute alcohol, concentrate this solution, and treat it with ether. A precipitate then falls, which cannot contain any other known sulphurous substance, and which we must fuse and deflagrate with nitrate of potash and caustic potash free from sulphuric acid; if sulphuric acid be found in the residue, we may regard the presence of taurocholic acid as almost certain.

Unfortunately, substances in which it is of interest to detect small quantities of taurocholic acid, are seldom obtained in a state of perfect freshness, and the little taurocholic acid that was originally present is decomposed before we commence our investigations. When we suspect that this acid is present, and have detected biliary matter by Pettenkofer's test in the alcoholic extract, we may hope to find taurine in the aqueous extract, which, however, contains it in such small quantity, and often so intermingled with other substances, that its recognition, even under the microscope, is extremely difficult. We must not attempt to determine the presence of sulphur as a test for taurocholic acid or taurine in the aqueous extract, for this contains both sulphates and other sulphurous organic bodies.

Physiological Relations.

Occurrence.—From the determinations of the amount of sulphur, instituted by Bensch* and others, we may conclude that taurocholic acid exists not only in the bile of the ox, but in that of the fox, bear, sheep, dog, wolf, goat, and certain birds and fresh-water fish; it has been found in the bile of the frog by Kunde and myself; and that it exists in human bile can hardly be doubted, since, as Gorup-Besanez was the first to prove, taurine may be exhibited from it. It might almost be inferred, from the numerical results obtained by Schlieper† in his analysis of the purified bile of a *Boa Anaconda*, that the liver of this serpent secretes taurocholic alone, and none of the other known biliary acids. That this acid is almost entirely absent in the bile of the pig, as shown by the investigations of Strecker, has been already mentioned.

Unchanged taurocholic acid has not yet been found in any other animal fluid; but from the experiments of Kunde to which I have already referred (p. 227), it is not improbable that it also occurs in the blood.

Origin.—We have very little to say in the present place regarding the production of taurocholic acid: what has been already stated respecting the formation of cholic acid (p. 126), of taurine (p. 182), and of glycocholic acid (p. 227), is equally applicable to the acid under consideration. As it has not yet been found in the blood, it is impossible to decide chemically whether it be primarily formed in the liver from its proximate constituents, or whether it proceeds from the general metamorphosis of the non-nitrogenous and nitrogenous animal matters.

Uses.—Since we are as ignorant of the chemical changes which taurocholic acid undergoes in the intestinal canal, as we are regarding those of glycocholic acid, we are unable to express by a chemical equation, the part which it takes in the process of digestion; and until this can be done, we cannot give a satisfactory explanation of the *chemical* action of the bile. The consideration of the *physiological* relations, from which we judge of the importance of the biliary secretion, in reference to the metamorphosis of the animal tissues and to animal life, and which is based on the chemical substratum we have here laid down, will be found in another part of this work.

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* Ann d. Ch. u. Pharm. Bd. 65, S. 194-203.

† Ibid. Bd. 60, S. 109-112.

HALOID BASES AND HALOID SALTS.

The consideration of the above series of organic acids has made us become acquainted with a number of bodies, which, in opposition to the ordinary rules of chemistry, enter into combination with acids without depriving them of their most essential chemical characters. There is, however, also a series of substances which can so combine with organic and mineral acids, that they perfectly neutralise their acidity, and can form with them true salts, both neutral and acid, without deserving, on account of their containing no nitrogen, to be classed among the alkaloids.

This class of salts has recently been referred to the conjugated compounds (by Gerhardt and Laurent,* and Strecker,†) since the idea of bodies of this nature has become tolerably firmly established; but the property of these non-nitrogenous bases, perfectly to saturate the strongest mineral and organic acids, appears to us a very stringent reason why these bodies should be separated from the true adjuncts, and why their neutral and acid combinations with acids should be separated from the true conjugated acids. Berzelius‡ has applied the name of *Haloids* to these salt-like combinations of acids with non-nitrogenous bodies. If we attempt to apply the highly probable (but not indubitably established) hypothesis of conjugated ammonia, to explain the basicity of the true nitrogenous alkaloids, we shall find such a mode of explanation perfectly inapplicable to these non-nitrogenous bases. These haloid bases may be classed as analogous bodies to oxide of ammonium. For as, according to the ammonium-theory of Berzelius, we assume, in the so-called ammonia-salts, the existence of the oxide of a combination of nitrogen and hydrogen, H_4N, in which this in some degree simulates a metal, so also we are equally justified in seeking for the basicity of these substances in the oxide of a carbo-hydrogen; and more especially since we are already acquainted with pure carbo-hydrogens possessing decided basic properties, as, for instance, the non-oxygenous ethereal oils. This assumption is not in the least opposed by the circumstance that the carbo-hydrogens, like the ammonium, combine with oxygen to form basic oxides. It is true that such a mode of viewing the subject leads us back to the frequently attacked, but by no means perfectly controverted or exploded theory of organic radicals; but, in a department of science so young as chemistry still is, that is the most satisfactory mode of contemplating the subject, which enables us to represent and explain, in the simplest manner, the largest number of analogous phenomena.

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* Ann. d. Chim. et de Phys. 3 Sér. T. 24, pp. 163-208.

† Ann. d. Ch. u. Pharm. Bd. 68, S. 47-55.

‡ Jahresber. 27, S. 425.

These oxides of the carbo-hydrogen radicals are, however, in their isolated state, so different from the known mineral bases and organic alkaloids, and exhibit such weak basic properties, that for a long period it was altogether denied that they possessed the character of a base. It is with difficulty that they combine either with acids or with water. Even their hydrates differ so greatly from the anhydrous oxides, that they were formerly regarded as perfectly different bodies, and ether was carefully distinguished from alcohol, oxide of amyl from fusel oil, and oxide of methyl from pyroxylic spirit. Moreover, it is only with difficulty, and in certain instances, that we can separate the water from these hydrates. In the same way, their combinations with acids, although most of them are perfectly neutral, bear very little resemblance in their character to salts, and hence most of them have received trivial names, as, naphthas, fats, &c.

As has been already mentioned, the haloid bases form neutral as well as acid salts; in the former the acidity of the stronger acids is, for the most part, far more perfectly neutralised than in the salts of the nitrogenous alkaloids; for the neutral salts, with a few exceptions, exert no action on litmus; they are, however, essentially distinguished from the salts of almost all other known bases by the circumstance that they cannot be so readily separated from their acids by simple or double elective affinity. The haloids cannot be decomposed by stronger acids, nor yet by stronger bases; it requires a more considerable time and a more prolonged action of heat to resolve them into their proximate constituents, than is necessary for ordinary salts.

In these decompositions of the haloid salts we constantly find that the base, during its liberation, combines with water, and is thus separated as a hydrate (for instance, not as oxide of ethyl but as alcohol, not as oxide of methyl but as pyroxylic spirit, not as oxide of lipyl but as glycerine). Conversely the haloid bases in uniting with acids give off all their water, so that they always form perfectly anhydrous salts—a fact of which chemists have long availed themselves, in order to ascertain the composition of organic acids in the anhydrous state; (the combinations of such acids with oxide of ethyl or oxide of methyl, being submitted to examination.)

We should fall into a great error if we were to conclude from the peculiar relations of the haloids that organic bodies are constituted on entirely different principles from mineral bodies; for the chemical laws deduced from pure inorganic compounds meet with their fullest application in these compound organic matters; it is, however, inorganic chemistry which teaches us, that the smaller the chemical attraction between two substances, with so much the more difficulty can they combine with one another, but when once combined, they often resist the most powerful decomposing agents; we need only refer by way of illustration, to the relations of silicic and phosphoric acids to alumina and zirconia. A natural law admits of no exceptions, and if the principles taking their origin in inorganic chemistry be true natural laws, they must be applied in their fullest extent to the chemical combinations of organic matters.

The true nature of the acid salts of the haloid bases was also for a long period not recognised; these substances were regarded as peculiar acids, whose consideration led indeed very materially to the theory of conjugated acids and conjugation; but there is an essential difference between an acid haloid salt and a conjugated acid. We have already seen that in the conjugated acids, the true acid has lost none of its saturating capacity, while in these acid haloids half of the acid is always saturated by the haloid base: we know, for instance, that sulphovinic acid cannot, by any possibility, be regarded as a conjugated acid, since only half of the sulphuric acid contained in it is in a state to saturate a base, just as in bisulphate of potash only half of the acid can be engaged in saturating the base. Notwithstanding this very striking difference, many of the acid haloid salts are, unfortunately, still ranked amongst the conjugated acids.

Moreover, these acid salts are distinguished from the other known acid salts of other bases by the difficulty with which the true base can be separated from the compound; indeed, the separation is here, for the most part, more difficult to accomplish by strong affinities than in the neutral haloid salts. The acid haloids have, however, very many properties in common with one another; they are either solid and crystallisable, or liquid, and, like most of the acid salts in mineral chemistry, always contain 1 atom of water from which they cannot be separated without total decomposition, except by means of a base; further, however volatile the acid and the base may be, these acid salts cannot be distillled or sublimed undecomposed; and, lastly, it is worthy of remark that their combinations with bases are almost without exception soluble in water, even though the acid in question formed ever so insoluble a salt with a base, (as, for instance, in the case of sulphate of oxide of ethyl and baryta.)

Amongst the haloid bases there is a series of homologous bodies of high interest in relation to theoretical chemistry, but scarcely falling within the sphere of zoo-chemistry. These are the bodies already mentioned in p. 40, possessing the general formula $C_nH_{n+1}O$, and standing in a definite relation to the acids of the first group.

There is, however, another haloid base of more importance in zoo-chemistry, but homologous to no other body with which we are acquainted, the *oxide of lipyl*, which, in combination with the fatty acids, constitutes the fats which hold so prominent a place in physiological chemistry. There are many other haloid bases, but for the most part only some of their combinations, namely, their acid salts, have been examined; and in their isolated as well as in their hydrated state they are yet unknown. Hence, we have here only to consider *oxide of lipyl* and its combinations, and *oxide of cetyl*, which is homologous to the group of ethers.

OXIDE OF LIPYL.—C_3H_2O.

On boiling one of the common fats or fatty oils with a caustic alkali, with the hydrate of an alkaline earth, with hydrate of magnesia, or oxide of zinc or of lead, the fat, without assimilating oxygen, or giving off hydrogen, is decomposed into one or more *fatty acids*, which combine with the base that has been employed, and form *soaps*, and a peculiar sweet matter, *glycerine*. On comparing the weight of the resulting products of decomposition with that of the fat which was employed, we find that an increase of weight has taken place in consequence of an assimilation of water.

In order to explain the nature of this process, it was assumed that the fats are combinations similar to the salts of oxide of ethyl, and that glycerine, represented by the formula C_3H_2O, constituted the base of the fats; but the constitution of glycero-sulphuric acid proves that glycerine must be represented by the formula $C_6H_7O_5$, and that consequently it cannot be regarded as the base of the neutral fats. Hence it is probable that the fats contain, in addition to the fatty acid, the oxide of a radical, having the composition which was formerly ascribed to glycerine; and that this oxide in its separation from the fatty acid assimilates water, and is converted into another body, as in the case of oxide of ethyl when it is expelled by an acid from its combination. To this hypothetical radical, Berzelius has applied the name of *lipyl*.

That the base in the fats is not glycerine seems obvious also from the circumstance that hitherto no neutral fat has been prepared from glycerine and the fatty acids. Whether the butyrin that has been artificially formed from glycerine and butyric acid has the same composition with that contained in butter has not yet been ascertained. Acrolein, which is polymeric with oxide of lipyl, and is a product of distillation of glycerine, cannot, any more than glycerine, be the base of the fats, since it cannot be made to combine even with strong acids.

This conversion of the fats into acids and glycerine, may be induced by other bases than those we have already mentioned, namely, by the soluble carbonates and borates, if they be digested with the fats for a sufficiently long period.

In the case of the carbonates we must, however, suppose that in this process the alkaline carbonate is first resolved into alkaline bicarbonate and free alkali, and that it is the latter only which takes part in the saponification; and that, on further boiling, the alkaline bicarbonate loses 1 atom of carbonic acid, and becomes converted into a simple salt, which again acts on the fat in the above described manner.

Ammonia and its carbonate only form soaps after a more prolonged action.

GLYCERINE.—$C_6H_7O_5.HO$.

Chemical Relations.

Properties.—Glycerine is a faintly yellow fluid with an agreeable, sweet taste; it attracts water from the atmosphere, dissolves readily in water and alcohol, but not in ether, and exerts no reaction on vegetable colours. It dissolves alkalies and several of the metallic oxides (for instance, oxide of lead) in large quantities; in a concentrated state, it admits of being distilled with only partial decomposition, but when rapidly heated, it is entirely decomposed; if its watery solution be exposed to evaporation, decomposition immediately commences: when heated in the air, it becomes inflammable, and burns with a blue flame. If heated with anhydrous phosphorus in a tube from which fresh air is excluded, it yields acrolein. If glycerine be dissolved in a large quantity of water, mixed with yeast, and exposed to a temperature of between 20° and 30°, it developes a small quantity of gas, and is converted into metacetonic acid ($C_5H_7O_5 - 2HO = C_6H_5O_3$; Redtenbacher.[*]) Treated with spongy platinum, glycerine also becomes converted into an acid (Döbereiner[†]). By concentrated nitric acid it is converted into carbonic acid, oxalic acid, and water; with hydrochloric acid and peroxide of manganese, it yields a large quantity of formic acid.

Composition.—In accordance with the above formula deduced by Pelouze[‡] from his analyses of pure glycerine and its acid salts, this substance consists of:

Carbon	6 atoms	39·130
Hydrogen	7 „	7·609
Oxygen	5 „	43·478
Water	1 „	9·783
		100·000

The atomic weight of anhydrous glycerine = 1037·5.

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[*] Ann. d. Ch. u. Pharm. Bd. 57, S. 174-177.

[†] Journ. f. pr. Ch. Bd. 29, S. 451.

[‡] Compt. rend. T. 21, pp. 718-722.

Glycerine cannot be regarded as a hydrate of oxide of lipyl, because in its combinations it always contains 3 atoms of water more than a double atom of oxide of lipyl; and we know that no haloid base retains its hydrate-water when it combines with acids.

Combinations.—No neutral salts of glycerine have yet been exhibited, but we are acquainted with several of its acid salts, which, like the acid salts of the oxides of ethyl and methyl, unite with bases, and form a series of compounds.

Bisulphate of glycerine (*glycero-sulphuric acid*) $C_6H_7O_5.SO_3+HO.SO_3$, is formed by the direct union of glycerine with sulphuric acid; the excess of sulphuric acid is removed by saturating with carbonate of lime or baryta; the sulphate of glycerine-lime or glycerine-baryta is decomposed with oxalic acid and the filtered fluid evaporated *in vacuo*.

This acid salt forms a colourless fluid, which, on evaporation even *in vacuo*, is readily decomposed into glycerine and sulphuric acid; it has a strongly acid taste, reddens litmus, and forms easily soluble double salts, even with baryta and lime. These salts readily yield glycerine when boiled, and even more readily when treated with an excess of base; the dry salts when heated carbonise and develope a vapour (containing acrolein) with an extremely disagreeable odour, and irritating to the eyes. The lime-salt crystallises in colourless needles, and $=CaO.SO_3+C_6H_7O_5.SO_3$.

Acid phosphate of glycerine, (*glycero-phosphoric acid*,) $C_6H_7O_5.2HO+PO_5$, is obtained by the direct action of syrupy glycerine on pulverised glacial phosphoric acid, which developes much heat, the temperature even rising to 100°. The excess of phosphoric acid is removed by baryta, and the baryta-salt decomposed by sulphuric acid. When in a concentrated state the body in question forms a colourless fluid, which even *in vacuo* cannot be very strongly concentrated without undergoing decomposition; it does not crystallise, has a strongly acid taste, and dissolves freely in water and alcohol; with bases it forms double salts, which dissolve readily in water, but so very slightly in alcohol that this fluid precipitates them from their aqueous solutions. *Phosphate of glycerine-lime*, $2CaO+C_6H_7O+PO_5$, crystallises in white, glistening scales, and dissolves in cold water; it is, however, so slightly soluble in hot water that it is precipitated from its aqueous solution by boiling. The baryta-salt contains 1 atom of tribasic phosphoric acid, 2 atoms of baryta, and 1 atom of glycerine.

Bitartrate of glycerine, $C_6H_7O_5.C_4H_2O_5+HO.C_4H_2O_5$, is produced, according to Berzelius,* on heating 1 part of glycerine, dried at 120°, with 2 parts of dry tartaric acid; it is a semi-solid transparent body, which is solid at 0°, but at 25° admits of being drawn out in long threads; it deliquesces in the air, does not dissolve in alcohol, and with bases forms soluble uncrystallisable double salts, which are readily decomposed by an excess of base. The relations of *biracemate of glycerine* are similar to those of this salt.

Products of its metamorphosis.—Acrolein, $C_6H_4O_2$, discovered by Redtenbacher,† is obtained from glycerine by submitting it to dry distillation with a little anhydrous phosphoric acid in a stream of dry carbonic acid gas; the distillate, consisting of a thick oil, of an acid fluid swimming on it, and of acrolein floating on the latter, must be digested with oxide of lead and distilled at 52° into a receiver containing carbonic acid, by which means we obtain the acrolein. It is an oily fluid, which strongly refracts light, has an acrid, burning taste, irritates the eyes and respiratory organs, and forms a neutral solution in water devoid of air, which, however, very soon assumes an acid reaction on exposure to the atmosphere. It instantly reduces oxide of silver, and it decrepitates both with nitric acid and with potash.

Acrylic acid, $C_6H_3O_3+HO$, is formed when acrolein is oxidised either by exposure to the air or by oxide of silver ;it is a limpid fluid, with an odour resembling that of very strong acetic acid, and a pure, acid taste; nitric acid converts it into acetic and formic acids; it forms soluble, crystallisable salts with bases.

Disacrone, disacryl, $C_{10}H_7O_4$, is gradually deposited from acrolein exposed to the atmosphere; it is idio-electric, devoid of odour and taste, and insoluble in all *menstrua.*

Preparation.—Glycerine is formed, as we have already mentioned, during the saponification of the fats, from the oxide of lipyl contained in them combining with 4 atoms of water. It is usually prepared from the aqueous fluid which separates during the preparation of lead-plaster, and contains it, together with oxide of lead, in solution. After the removal of the lead by sulphuretted hydrogen we concentrate the solution first in the water-bath and subsequently *in vacuo.* We may also obtain it from the mother-liquid yielded in ordinary saponification by the alkalies, on saturating the alkali of the ley with sulphuric acid, then heating it with carbonate of baryta, evaporating the filtered fluid, and extracting with alcohol. It may be obtained very readily, and in a state of purity, by dissolving castor-oil in absolute alcohol, and passing hydrochloric acid gas through the fluid; at the end of the operation the compounds of the fatty acids with oxide of ethyl, which have been produced, must be separated by means of water. The aqueous fluid, on evaporation, leaves glycerine, which may be entirely freed from adhering traces of the fatty ethers by being shaken in ether.

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* Jahresber. Bd. 27, S. 438.

† Ann. d. Ch. u. Pharm. Bd. 47, S. 113-148.

Tests.—Glycerine could not be readily detected in animal fluids unless we were able to obtain it in sufficient quantity to admit of its being subjected to an elementary analysis; but this would be hardly possible, since it would be difficult to obtain the glycerine in a state of purity from the animal fluids. Fortunately, however, acrolein is a substance with so intense and characteristic an odour that this product of the decomposition of glycerine may be employed as a test of its presence. The glycerine, separated in as pure a state as possible, must be rapidly heated either alone or with a little anhydrous phosphoric acid, when, if the glycerine be much diluted, the peculiar and very disagreeable odour, not unlike that developed by the wick of an expiring oil-lamp, is evolved with sufficient distinctness.

Physiological Relations.

Occurrence.—Glycerine has been recently discovered by Gobley* in animal bodies. He first detected it in the *yolk of the egg* of the common fowl in the form of phosphate of glycerine-ammonia, and subsequently† in the same state of combination in the *fats of the brain.*

Origin.—Regarding the source of the glycerine in the organism, there can be no doubt that, in addition to the true fats—the stearate, margarate, and oleate of oxide of lipyl—there are many fatty acids, either free or in combination with alkalies, occurring in the animal body. Since the combinations of the fatty acids and oxide of lipyl are introduced into the animal body from without, we need not wonder that glycerine, which is formed from oxide of lipyl during the decomposition of the fats, is not found in far larger quantity in this or that animal fluid. We have already directed attention to the possibility (p. 56 and p. 103) that in the consumption and gradual oxidation of the neutral fats, the oxide of lipyl, separated as glycerine, is probably converted into lactic or even into metacetonic acid. Further investigations are, however, necessary before we can decide whether this conjecture is of any real value. The uses of fatty articles of food would thus assume a new aspect, since they would in this way contribute to the formation of the free acids which act so important a part in many of the processes of animal chemistry.

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* Compt. rend. T. 21, pp. 766-769, et 988-992.

† Journ. de Pharm. 3 Sér. T. 11, pp. 409-417, et T. 12, pp. 5-13.

How the glycerine in the yolk of egg and in the brain becomes associated with the phosphoric acid, we cannot specially explain, but, considering the frequency with which phosphorus occurs, both in its unoxidised state and as phosphoric acid, there is nothing singular or inexplicable in such a combination.

SALTS OF OXIDE OF LIPYL.—FATS.

Chemical Relations.

General Properties.—It is especially worthy of remark that the properties of these haloids are almost entirely influenced by the acids contained in them; while in the salts of oxide of ethyl, most of the properties, including those of the most general character, appear to depend principally on the base, and to be altogether independent of the nature of the acid. Hence we find the properties of the neutral fats to be extremely similar to those of the fatty acids already described (from p. 105 to p. 116.)

Most of the animal fats are soft and greasy at an ordinary temperature, although some are firm and waxy, and a few liquid; they almost all correspond, however, in the following points. When exposed to strong cold, especially when in solution in alcohol, they may be obtained in white scales or minute plates of a peculiar lustre; when perfectly pure, they are for the most part colourless and transparent, they swim on water, render paper and linen transparent, are bad conductors of electricity and heat, melt for the most part below the boiling point of water, are altogether decomposed when distilled, unless the process be conducted *in vacuo*, and are devoid of smell and taste when they are pure and fresh; they are insoluble in water, but most of them dissolve in boiling alcohol, from which they again separate on cooling; they are all soluble in ether and in volatile oils; when perfectly pure they exert no reaction on vegetable colours, but on exposure to the air many of them readily become rancid and acid from the absorption of large quantities of oxygen. When exposed to a strong heat, and free access of oxyen is admitted, they are inflammable, and burn with a clear flame.

There are certain ferments which resolve the fats into glycerine and the corresponding fatty acid, in the same manner as sugar is resolved into alcohol and carbonic acid, or salicin into saligenin and sugar, or amygdalin into sugar, hydrocyanic acid, and oil of bitter almonds. Albuminous substances which have already undergone a certain degree of decomposition (putrefaction) act in this manner as ferments to the fats.

If we mix putrid fibrin, which forms an albuminous fluid, with water, or putrid casein with fat, so as to form an emulsion, and digest the mixture for some time at a temperature of 37°, the corresponding fatty acids separate from the oxide of lipyl, which very soon undergoes further alterations. In the fermentation of milk, where sugar is present, it appears from my investigations* that the fats are decomposed in precisely the same manner as if merely the putrefying protein-compounds were acting as ferments, and as if no sugar were present. Cl. Bernard† on digesting fats with pancreatic fluid observed that they were decomposed into fatty acids and glycerine, from which he concluded that during the act of digestion the fats are constantly decomposed into glycerine and fatty acids—a conclusion, however, still admitting of considerable doubt.

By *dry distillation* certain fats yield other fatty and inflammable substances, and leave a little charcoal; others are in part converted into peculiar fatty acids. When very rapidly heated or thrown on incandescent bodies, they carbonise and develope olefiant gas.

The fats are decomposed by prolonged contact with *chlorine, bromine,* and *iodine;* while, on the other hand, they take up sulphur, selenium, and phosphorus, without undergoing any change; with the former, they only undergo decomposition on the application of heat.

By concentrated *mineral acids* they are for the most part converted into fatty acids, and on the application of sulphuric acid, they yield acid sulphate of glycerine.

Stearate of oxide of lipyl, stearin, occurs as a pure white substance; it separates on cooling from its alcoholic solution in snow-white, glistening scales; under the microscope it appears chiefly in the form of quadrangular tablets, which although almost square are, according to Schmidt,‡ rhombs with angles = 90° 5′, but sometimes in the form of short rhombic prisms (thick rhombic plates,) whose surfaces, according to Schmidt, are inclined to one another at angles of 67° 40′ and 52° 40. It melts at +62°, solidifies, but does not become crystalline on cooling, is brittle, when dry is not a conductor of galvanic electricity, is insoluble in cold and only slightly soluble in hot alcohol, but dissolves very readily in ether. On dry distillation it yields stearic and margaric acids, and the products of decomposition of glycerine; on saponification it yields stearic acid and glycerine.

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* Simon's Beitr. Bd. 1, S. 63-76.

† Arch. génér. de méd. 4 Sér. T. 19, p. 73.

‡ Entwurf u. s. w. S. 84.

Margarate of oxide of lipyl, margarin, is white and solid; it crystallises from alcohol as a flocculent white powder, which under the microscope appears in the form of very delicate and often curved needles, which are so grouped as to radiate from one point as a nucleus, and thus to form a whorl of fine, capillary threads; it melts at +48°, and dissolves slightly in alcohol but readily in hot ether; it separates from either solution on cooling in nacreous scales, and on saponification yields glycerine and margaric acid.

Oleate of oxide of lipyl, olein, or *elain,* is a colourless oil which solidifies at a low temperature, is not a conductor of galvanic electricity, becomes rancid on exposure to the air, is never entirely free from margarin and stearin, and on saponification yields, in addition to glycerine and oleic acid, a much larger quantity of margaric acid than can be supposed to be derived from the decomposition of the margarin.

Preparation.—The above fats may be obtained in various ways, although seldom in a state of perfect purity, from the fat contained in cellular tissue, by repeated melting and purification with water. Usually we dissolve the fat in boiling alcohol, from which, on cooling, the stearin, and a great part of the margarin, separate in crystalline scales, while the olein is almost the only substance remaining dissolved in the cold alcohol. Margarin is obtained in the greatest purity from the hot alcoholic solution of those fats, which, like human fat and the vegetable fats, contain no stearin; moreover, by strong pressure between the folds of filtering paper, the olein may be tolerably effectually separated from the stearin and margarin, since, above a certain temperature, it penetrates the paper. Tolerably pure olein may be obtained by digesting a fat with half the quantity of potash required for its complete saponification; in this case the stearin and margarin are saponified, while the olein remains unchanged. The corresponding acids may be obtained in a similar way, but in a state of much greater purity.

Tests.—Cases sometimes present themselves in which it is not easy to ascertain whether the substance to be examined contains salts of oxide of lipyl, or the corresponding fatty acids. In dealing with small quantities, we obviously cannot rely on the acid reaction, or on the formation of glycerine; in such cases the simplest method is to obtain an ethereal extract of the alcoholic extract to which a little acetic acid had been added, and then, by digestion with water, to separate the residue of the ethereal solution from other substances. The remaining fat is then to be dissolved in alcohol, and to be treated with an alcoholic solution of acetate of lead. If the addition of ammonia give rise to no precipitate, it is a proof that the solution contains no free fatty acids, but only salts of oxide of lipyl.

Free fat in the animal fluids, tissues, and cells, is most commonly and, indeed, most satisfactorily detected by the microscope; the vesicles in which fat ordinarily appears, present so characteristic an appearance, that when they have been seen for a few times under the microscope, they can hardly be confounded with anything else; the more consistent fat, containing little olein, sometimes, however, occurs in nodular, sausage-shaped, and only faintly-transparent clumps, which cannot so readily be recognised as fat. In these cases, chemistry must come to the aid of microscopic investigation, as, for instance, where the fat-vesicles in cells are so minute, that, with the highest magnifying powers, they appear as mere dark points or granules. Many histologists now maintain that these points and aggregate granules may be very readily distinguished under the microscope, by their solubility in ether; but the extraction of the fat from the cells by ether, is by no means easy, for its rapid evaporation under the microscope, renders it very difficult, if not impossible, to observe the individual cells. Before making our observations we must, therefore, repeatedly pour a little ether on the object, and allow it again to run off, or if we have fine sections of tissue, we may digest them in ether. Unfortunately however, the cells and other histological elements are often so distorted by ether, that even after long maceration in water, an accurate observation is no longer possible; and it is nearly the same in most cases with alcohol, by which, however, well-prepared sections of many parts, as, for instance, nerve-fibres, may often have their fat thoroughly removed. Moreover, alkalies cannot be advantageously applied to the partial saponification of these fats, since they often dissolve albuminous parts much sooner than the fats. We shall see, in a future part of this work, that some histologists believe that they have found fat-granules in tissues which have been hitherto regarded as utterly devoid of fat; and have been too hastily led, by imperfect experiments, to form theories regarding the fatty degeneration of cells and tissues.

Physiological Relations.

Occurrence.—Fats occur, not only in the animal world, but also in vegetables, especially in seeds and the kernels of fruits, from which we chiefly obtain the fatty oils and certain butter-like fats, as for instance, cacao butter, palm oil, &c. Fats have been found in almost all parts of all animals, and it is only in the lowest classes of animals that fat is entirely absent. It is in the higher organisms that we find most fat, where it exists as a mixture of the above-named salts of oxide of lipyl, and is deposited in the cellular tissue in oval or polyhedric cells.

It is very rarely that we find one of the above-named fats unmixed with the others, and in the few cases of this nature which have been observed, the character of the fat has been recognised by the microscope only, and not by chemical means; thus C. Schmidt (according to Bergmann*) and Vogt† found distinct crystals of stearin in the ovum of the frog, and of the accoucheur toad, (*Bufo obstetricans*,) and I have frequently, although not invariably, found delicate masses of acicular crystals in the albumen of eggs that had been sat upon from three to six days, which from the few tests that I could attempt, seemed to consist of margarin.

When we consider the occurrence of fat in the different parts of the human body in a normal condition, we, in the first place, discover large accumulations of fat, which, when constituting an integral constituent of certain organs, rarely disappear entirely, even in the latest stages of wasting diseases; in the next place we observe, that there are parts of the body in which the quantity of fat varies considerably, being either extraordinarily small or very large; and finally, that there are some organs in which accumulations of fat are of very rare occurrence. The *orbit of the eye* and the heart appear to be the most constant seats of fat, for although we observe that the fatty matters surrounding the different parts of the eye diminish in all forms of disease, causing the eye-ball to sink in the orbit, the socket of the eye is never found entirely free from fat. A similar remark applies to the fat surrounding the *heart*, and penetrating between its bundles of fibres; and it would likewise appear that fat is never entirely absent from the *muscles*

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* Müller's Arch. 1841. S. 89.

† Entwickelung der Geburtshelferkröte. Solothurn. 1842. Einl.

of the face, for every one who has dissected these muscles must have noticed how largely the human face is furnished with fat.

Large quantities of fat, not constituting so essential and integral a part of the organs, and often almost entirely disappearing, are principally found under the *cutis* and in the *cellular tissue*, investing the muscles, in the interstices of several of the larger muscles, about the glutæi, on the soles of the feet, and in the inner surface of the hands. Fat is frequently fo und deposited insacs around different *tendons* projecting between the ends of the bones into the joints, where they form special accumulations of fat, known by the name of the *Haversian glands.* Large deposits of fat are generally found in the *omentum*, and surrounding the kidneys, constituting the *folliculus adiposus renum*, which usually contains a harder fat, having a larger quantity of margarin, than occurs in other parts of the body.

The *female breast* is always so largely interspersed with masses of fat, that full prominent breasts frequently yield a small quantity of milk, being enlarged solely by the deposition of fat.

The *marrow of the bones* consists, for the most part, of fat, which not only remains undiminished, but is even not unfrequently largely augmented in various diseases of the bones, as, for instance, in *osteomalacia.* This bone-fat is perfectly identical with the ordinary fat of the cellular tissue, excepting that it contains somewhat more olein, especially where there is osteomalacia.

All other parts of the animal and more especially of the human body, are penetrated by fat. The smallest quantity, and indeed, occasionally, not a trace of fat is to be found in the *pulmonary tissue*, in the *glans penis* and the *clitoris*, and, if we except the so-called non-saponifiable fats, in the brain.

We have already spoken of the occurrence of fat in the *animal fluids.* The amount of fat in the *blood* does not vary much in a normal condition, and is, according to Boussingault's numerous investigations,* wholly independent of the amount of fat contained in the food. The blood contains from 0·14 to 0·33% of fat in a normal condition. Boussingault found from 0·2 to 3·0% of fat in the blood of dogs, whether they had partaken of food deficient or abounding in fat, and 0·4% in that of birds. Tiedemann and Gmelin always found the *chyle* very rich in fat; and its milky turbidity, as well as that of the *lymph*, is owing to the fats which it holds in suspension.

I was unable to discover any trace of Boudet's *serolin* in the chyle of a dog. The fat which was extracted with ether was oily, was not precipitated from boiling alcohol on cooling, and was for the most part saponifiable.

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* Ann. de Chim. et de Phys. 3 Sér. T. 24, p 460.

This seems to confirm Schultz's observation,* that the fat of the blood is more consistent than that of the chyle, and it may further be remarked that the fats of the blood are mostly saponified or incapable of saponification, while those of the chyle correspond to the ordinary salts of oxide of lipyl.

The excellent investigations recently instituted by Cl. Bernard† have afforded the most striking proof that the fats are digested by the pancreatic fluid; *i. e.*, that the fats are not reduced to an emulsive state, either by the gastric juice, or (as Brodie‡ believed that he had found) by the bile, and thus fitted for resorption. But the conclusion which Bernard would draw from an experiment in which he found that fat had been converted into fatty acids and glycerine by the action of the pancreatic juice, viz., that all fats are converted by the process of digestion into glycerine and the corresponding fatty acids, is controverted by the fact above referred to, that the chyle contains, in comparison with the blood, much unsaponified and but little saponified fat.

Marchand and Colberg found oily and crystalline fat in the lymph.

The quantity of fat in the human body varies considerably at *different periods of life.* Thus in the fœtus we generally find no fat, except a few small masses in the omentum and in the loins. Infants prematurely born are rounder in form immediately after birth than at a subsequent period, for as their organism is not fully prepared for an atmospheric life, they soon become emaciated, and lose much fat through the intestinal canal. The muscular tissues of the heart and face are found to be copiously furnished with fat even at this early period. New born children are in general tolerably plump and roundish, and have a considerable quantity of fat deposited under the skin. The organism is most rich in fat during childhood, but this deposition of adipose matter diminishes with the development of the sexual functions, although it again increases at a more mature period of life, and then occasionally acquires an excess never observed at any other age. Extreme old age gradually arrests this tendency to adiposity until it is completely destroyed by *marasmus senilis.*

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* System der Circulation, 1836. S. 131.

† Arch. génér. de méd. 4 Sér. T. 19, pp. 60-81.

‡ Quart. Journ. of Science. Jan. 1823.

A merely superficial comparison of the *sexes* shows that the female organism contains more fat, and has a greater tendency to the deposition of fatty matter than the male, as indeed is most evident from the rounded outlines and symmetrical curves of the female figure, which cannot be entirely destroyed even by influences most inimical to the deposition of fat.

We find that special physiological relations give rise in some cases to an increase, and in others to a diminution of the fat in the animal organism. Thus an excessive *activity of the sexual functions* prevents the increase of fat, and even induces considerable emaciation where the sexual activity is of a morbid character. Men and animals that have been castrated, are, on the contrary, much disposed to become fat, as are also women who have ceased to conceive. Many male animals, according to Haller, lose the marrow from their bones in the season of heat.

It is well known that great *muscular activity* not only impedes, but even utterly arrests the deposition of fat. Thus the flesh of the Arabs, and that of all nations living in a state of nature, as well as of most wild animals, contains a very small quantity of fat, while civilized nations and the domestic animals reared for purposes of food are, in general, much fatter, owing to their inconsiderable muscular activity. Most persons are familiar with the fact that horses become much leaner in summer even when better fed, and that they soon grow fat in the winter. The whole art required in fattening domestic animals consists in suffering them to have little exercise and good feeding.

We have daily opportunities of noticing the influence exercised by *food* alone on the deposition of fat; and the degree to which the *temperament* and *conditions of the mind* affect the corpulency or meagreness of the human body is too obvious to require further notice here.*

Every physician is familiar with the marvellous rapidity with which fat disappears from the animal body in acute as well as in chronic *diseases*, and we would here only refer to the fact which undoubtedly is well known to many physicians, that tuberculosis very frequently induces very little or no emaciation, even where the pulmonary tissue is already in a great measure destroyed, if the disease be accompanied with certain forms of hepatic disease, as fatty or nutmeg liver. The emaciation is often so inconsiderable in these cases, that any one not acquainted with the physical diagnosis of the disease, would be completely deceived as to its character and the amount of danger.

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* We may refer to the first volume of Haller's *Elementa Physiologiæ* for the most copious accumulation of facts bearing on this subject.

It appears scarcely necessary to remark that *milk* contains a larger quantity of fat than any other animal fluid. An average of 2·9% of fat has been found in woman's milk. This subject we shall however consider more fully in the second volume of this work, when we purpose treating of the increase and diminution of the fat contained in the milk of different animals under different physiological and pathological relations.

Since Güterbock's observations, attention has been directed to the quantity of fat contained in *pus*, which has frequently been found to amount to 5%.

As we have already remarked, the fat in the *blood* is mostly in a state of saponification; but in many diseases, the blood has been observed to contain large quantities of unsaponified fat. Since we purpose entering more fully into this subject when we proceed to the consideration of the morbid conditions of the blood, we will here only observe, that although, as is generally supposed, the blood of drunkards frequently presents large accumulations of free fat, this only occurs where there is already some hepatic disease, as for instance, granular liver, whether this be a mere secretion of colloid-like exudation accompanied with decrease of size in the liver, or that species of granular disease in which some of the hepatic lobules present scattered cells infiltrated with fat.

Pathological depositions of fat, either free or enclosed in cells, occur most frequently in the *liver*, but also in the *kidneys*, the *spleen*, in paralysed *muscles*, in the *heart*, and other organs, and occasionally (enclosed in a capsule) in *encysted tumours*. This fatty metamorphosis (as it is termed) of some of the organs, will be specially considered in the third volume of this work, in our remarks on the individual tissues and organs. It will be sufficient at present to remark that these so-called fatty degenerations of organs occur either without any previous exudation, by the direct deposition of fat in the tissues, the cells, or the areolar tissue, or, (as indeed is more frequently the case,) after resorption of the physiological or pathological tissues or exudations, are deposited in their place. The latter case occurs in paralysis of muscles, where they have undergone fatty degeneration, and in osteoporosis and osteomalacia, where the bones, rendered porous by the resorption of their mineral and organic parts, are found, as it were, swimming in fat; a similar process may occur in the fatty degeneration of the spleen and the kidneys, which many have attempted to explain as the third stage, or indeed, as the essential character of Bright's disease. The endeavour to explain such pathological processes by a perfect metamorphosis of albuminous and fibrinous exudations into fat, (that is to say, by a direct metamorphosis of the protein-compounds into fat,) is purely chimerical and unsupported by the slightest proof.

It is further an undoubted fact that in many *cells*, whether they be constituents of physiological tissues, or products of pathological exudations, fat occurs accumulated in large quantities, appearing under the form of vesicles, or more frequently of granules, as in the hepatic cells, in the granular cells in old apoplectic cysts, and in the analogous cells in the expectoration in confirmed chronic catarrh; but it is incorrect to suppose that all strongly tinged, punctuated granular cells, contain much fat: we will, however, postpone all further consideration of this subject to the third volume.

We have no accurate observations regarding the quantity of fat contained in the *fæces* in different diseases; and I will here only remark, that I have always found fat in the normal excrements, but more especially in the stools in diarrhœa; in most of the cases, in which observations have been made regarding an excess of fat in the fæces, we are unable to determine whether its increase be owing to the food, or to fatty medicines.

A firm margarin-like fat, has been frequently noticed as present in the excrements of diabetic patients (Simon,* Heinrich†), but I have never observed any decided increase in the quantity of fat in the fæces in diabetes; and the discharge of fat by the intestines, cannot therefore be regarded as a constant symptom.

It is equally difficult to form a correct opinion of the quantity of fat in the *urine*. No reliance is to be placed on the older observations, since the presence of fat in the urine was at that period often diagnosed, whenever, in consequence of an alkaline reaction, the urine was covered with a pellicle; this was regarded as fat, although consisting in reality of nothing more than earthy matters. Where the microscope shows fat-globules in the urine, they frequently, in women, arise from the external genitals. It is only in slow fevers that I have been able to confirm the old view, and often, but not invariably, to detect fat-globules. In the urine of pregnant women, which contains the so-called kyestein, I‡ have, however, always observed a soft buttery fat. I have never met with true milky, or chylous urine, where the turbidity and colour were owing to the presence of fat; for this species of urine seemed to owe its peculiar character to a large quantity of pus-corpuscles, held in suspension, which in all the cases I examined, originated in the kidneys, and were not dependent on vesical catarrh. Where milky urine has been found to contain a large quantity of fat, it may be owing, as in Rayer's case*, to milk that had been purposely added, in order to deceive the physician.

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* Beitr. Bd. 1, S. 408.

† Häser's Arch. Bd. 6, S. 306.

‡ Handwörterb. der Physiol. Bd. 2, S. 9.

It would be very important, in reference to the diagnosis of Bright's disease, if we could confirm the conjecture advanced by Oppolzer, that in this disease, at any rate when there is fatty degeneration of the kidneys, the urine contains fat. I have, unfortunately, hitherto been unable to confirm this conjecture, for even where a *post mortem* examination showed decided fatty degeneration of the kidneys, the urine exhibited no microscopic fat-globules, nor did the ether extract any trace of fat. In one case only, where the urine removed from the bladder after death, contained the well-known epithelium cylinders, could I discover fat-globules. I cannot concur with Virchow in his opinion, that the strongly tinged epithelium of the tubes of Bellini contains fat, or that such cells are to be regarded as evidences of the existence of fatty degeneration.

Origin.—When we consider that vegetable food contains a greater or lesser quantity of fat, and that we find large quantities of the most ordinary vegetable fats accumulated in the animal organism, we might be disposed to infer that a vegetable diet was fully adequate to the nourishment of animals, since it has been discovered, or rather demonstrated, that it contains sufficient quantities of albuminous substances to compensate for the waste of the nitrogenous tissues. This view is daily confirmed by anatomical as well as purely physiological observations and experiments. Every farmer is well aware that cows will yield more butter when kept upon food abounding in fat, than when kept on fodder deficient in that ingredient, and that in rainy seasons, when plants contain less fatty matter, cows, although yielding large quantities of milk, give less butter than in dry seasons, although their food may be rich and good. If two organisms, similar in all respects, and under similar relations, partake of food differing in its quantity of fat, there will be a difference in the deposition of fat. It cannot be doubted that a large portion of the fats passes from the food into the blood; we need only observe the chyle when the food has been of a fatty character, to convince ourselves, by the presence of fat-vesicles, that it has been converted into a perfect emulsion, whilst it will present only a slight turbidity from the presence of lymph- or colourless blood-corpuscles, when the food has contained but little fat. Boussingault* even succeeded, by a series of ingenious experiments, in showing that only certain quantities of fat passed in a given time from the intestinal canal into the general system, and that the excess of fat was discharged unchanged with the excrements. Thus he observed in the case of ducks, that a duck, when kept on the fattest food, could not assimilate more than 19·2 grammes of fat in twenty-four hours (or 0·8 of a gramme in one hour), from the *primæ viæ*.

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* L'Experience, 1838. No. 42.

A sharp contest has been obstinately maintained during the last ten years in reference to the question whether the animal organism does not possess the capacity of generating the requisite quantity of fat from other nutrient substances besides preformed fat. Dumas, Boussingault,† and some other French enquirers,‡ have endeavoured to show by direct experiments, that herbivorous animals take up sufficient fat with their food, and that the animal organism has therefore no need of generating fat; while Liebig and his school§ have arrived at a totally different conclusion from observations of a precisely similar character. For as they found that certain animals contained more fat, and discharged a larger quantity in their milk and excrements, than they had obtained by their food, they were led to the conclusion that the animal body must possess the property of forming fat from other organic substances. The contested point unfortunately long remained undecided, since the two parties differed in their idea of that which they termed fat in the food; the French enquirers regarding as fats all the matters that can be extracted from plants by ether, and Liebig reasonably enough considering those matters only as fats which possessed all other properties of fats besides that of solubility in ether. Liebig appealed in support of his views to the experiments first made by Huber, and afterwards repeated by Gundelach, and which appeared to prove that bees, when fed on pure sugar, are capable of generating wax. Subsequently, Dumas, in conjunction with Milne

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* Ann. de Chim. et de Phys. 3 Sér. T. 19, pp. 117-125, et T. 25, pp. 730-733.

† Ibid. T. 12, p. 153.

‡ Persoz, in Compt. rend. T. 18, p. 245; Payen and Gasparin, in Compt. rend. T. 18, p. 797; Letellier, in Ann. de Chim. et de Phys. 3 Sér. T. 11, p. 433.

§ Playfair, in Phil. Mag. Vol. 22, p. 281.

Edwards,* found reason to believe that bees cannot be fed for any length of time on pure cane-sugar; but that when fed upon the honey yielded by this sugar, which contains a very little wax, they were able to produce that substance. Boussingault,† Persoz,‡ and others, have since that period convinced themselves, by repeated experiments on pigs, ducks, and cows, of the correctness of Liebig's view, and therefore this long-contested question may now be regarded as at rest.

But it must not be forgotten that these experiments have only been conducted on the statistical method (that is to say, by a comparison of the quantity discharged and the quantity taken up by the organism); and that they cannot therefore afford more than the general demonstration that under many relations, fat must be formed within the animal body. But the following questions still remain unanswered: Does the animal body continue to exercise its property of generating fat, when a sufficient supply has been conveyed to it by food? What is the true seat of the formation of fat? And finally, how, and by what process, and in what chemical proportion, is fat formed from starch or nitrogenous substances?

The first question, as to whether the organism *constantly exercises its power of forming fat,* does not admit of a solution in the present state of our knowledge, nor until a satisfactory answer can be given to the two other questions. If Boussingault's view be correct, that the ordinary vegetable substances contain sufficient fat to compensate for what has been lost through the functions of the animal body, we might infer that fat would only be generated from other substances when the food is deficient in fatty matters, or when the supply of fatty food is inadequate. It may, however, be argued against this teleological view, that if the conditions for the formation of fat are once present in the animal organism, this process will probably continue in operation without reference to the plus or minus supply of fat. But many pathological phenomena appear to show that this process may in some cases be abnormally excessive.

According to the views of Liebig and Scherer, in which most observers now concur, the *seat of the formation of fat* is to be sought in the *primæ viæ.* This hypothesis is not, however, based on strict proof, and its value greatly depends upon the origin we attribute to fat, namely, whether we derive it from albuminous, and therefore nitrogenous substances, or from starch, sugar, and other non-nitrogenous matters. Liebig's authority has given currency to the latter view, although it is opposed by many physiological facts. For if fat were formed in the *primæ viæ* from the starch of vegetables, the chyle would contain more fat after a vegetable than a fatty animal diet; but the contrary has invariably been noticed in all the observations made on this subject since the experiments of Tiedemann and Gmelin. Boussingault* moreover did not observe any instance in his recent experiments on ducks, in which the fat contained in the intestinal contents, was increased by feeding the birds on starch or sugar, although such must have been the case if a metamorphosis of these substances into fat occurred in this part of the system. Thomson† was also led by his experiments on the influence of different kinds of food on the production of milk and sugar, to adopt the opinion that sugar had no part in the formation of fat. The occurrence of hydrogenous gases in the intestines, and the well-known fact of the reduction of alkaline sulphates into sulphides during the process of digestion in the intestinal canal, might indeed seem to afford some grounds for the possible reduction of the substances containing carbon and the elements of water, to which we apply the term carbo-hydrates, viz., starch, sugar, &c.; but until supported by some conclusive evidence, this view must be regarded as scarcely tenable in opposition to the facts referred to. H. Meckel‡ was indeed led to believe, from some experiments made on the subject, that sugar was thrown into a sort of fermentation by the bile, and was thus converted into fat; but it had escaped the attention of Meckel, who regarded every substance that dissolved in ether as a fat, that his etherial extract contained not only fat, but all the products of decomposed bile soluble in ether; and the reason of his obtaining a larger quantity of ether-extract when the bile was decomposed by sugar, than when digested without sugar, was simply in consequence of the presence of the sugar, which very much promotes the decomposition of the bile, and the formation of products easily soluble in ether (namely free biliary acids.) It does not, therefore, appear from the facts already established, that fat is generated in the intestinal canal from sugar and starch, more especially as these substances would appear from Boussingault's experiments, to be too rapidly absorbed from the intestinal canal to allow of their being subjected to a fatty fermentation.

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* Ann. de Chim. et de Phys. 3 Sér. T. 14, p. 400.

† Compt. rend. T. 20, p. 1726.

‡ Ibid. T. 21, p. 20.

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* Compt. rend. T. 20, p. 1726.

† Ann. d. Ch. u. Pharm. Bd. 61, S. 228-243.

‡ De genesi adipis in animalibus. Diss. inaug. Hal. 1845.

Liebig has advanced an hypothesis, that fat may also be formed *from nitrogenous elements of food;* and this view would appear to acquire support from the experiments made by Boussingault on ducks. For the latter observer found that when these birds had been fed on albumen and casein, containing little or no fat, there was always more fat in their intestinal contents than when they had fasted for any length of time, or been fed only on clay, starch, or sugar. Unless, therefore, we would assume (which, indeed, we have no authority for doing,) that fat is secreted in the intestinal canal after the use of nitrogenous substances, we must admit, from the above experiments, that a portion of fat may be generated in the *primæ viæ* from albumen containing no fat. It must, however, be observed, on the one hand, that the increase of the fat in the intestinal canal, after the use of albuminous food, is very inconsiderable, and on the other, that the experiments are so few in number, that we have not sufficient *data* for the satisfactory solution of so important a question. But it is very possible that the digestion of nitrogenous food may be accompanied by a greater secretion of bile than that of non-nitrogenous substances, and that the fats and products of decomposition of the bile, may have increased the ether-extract of the contents of the intestine, in the above experiments, after the use of nitrogenous food. As has been already observed, the solid excrements presented scarcely any *residua* of the bile except those which are soluble in ether.

Since the above facts do not, as yet, justify us in assuming that the seat of the formation of fat must be sought in the *primæ viæ*, we must turn to the processes at work in the blood, unless, indeed, we freely confess that nothing definite can, at present, be advanced on this subject.

The third question, as to *how* fat is formed from other substances, would next engage our attention, if the preceding considerations did not show that we are entirely deficient in the materials necessary for affording a satisfactory answer. For, so long as we are ignorant of the grounds on which a process is based, although we may be acquainted with its individual factors, we must defer all idea of a scientific explanation; there is, however, no deficiency of imaginary schemes to explain the formation of fat from sugar or protein. Support has been borrowed from the somewhat irrelevant fact of the butyric fermentation of sugar and starch; but, as we have already observed, (p. 33,) there are no grounds for reckoning butyric acid among the fats, and the formation of metacetonic, acetic, and formic acids, may just as well be regarded as processes of the formation of fat, as that of butyric acid. We are, therefore, for the present, constrained to regard this view as a mere fiction, illustrated by chemical symbols, since, whatever corroboration it may acquire from future experiments, it is at present wholly devoid of all scientific support.

Uses.—We may regard the application of fat in the animal body as conducive to mechanico-anatomical, to physico-physiological, and chemico-physiological objects.

The uses of the fat deposited in the areolar tissue of the animal body are almost entirely of a strictly physical nature. If we reflect that fat is mostly found in a fluid state during life, we shall perceive some of the most useful properties which this condition imparts to the animal body. For although fat is enclosed in separate layers and cells, it possesses so great a degree of mobility as to propagate pressure equally in all directions in the same manner as water. Every physicist knows that a bladder perfectly filled with water cannot be brought to assume any given form without bursting; but we know that pressure applied to any part of such a body will be equally propagated in all directions. If, therefore, we suppose a number of such bladders to be laid side by side, enclosed in a larger space, and that we press one of them, the pressure thus applied will be propagated to all the others; and here we have an illustration of the uniform diffusion of external pressure through the whole adipose tissue. But besides the protection thus afforded the body from external shocks, it is further guarded in leaping and falling by the Haversian glands, which penetrate into the joints, and, receiving the shock, propagate it over a larger surface, by which its violence at each individual point must be very much diminished. Such was the object of nature in placing layers of fat on the soles of the feet, and the tuberosities of the Ischium; and thus the depositions of fat were made to answer the purpose of water-cushions and other inventions of man's ingenuity, for the promotion of his ease and comfort.

Haller was the first who drew attention to the extreme utility of fat in filling up those interstices which must unavoidably exist between muscles, bones, vessels, and nerves. The bodies of children and women principally own their rounded forms to the deposition of fat in the subcutaneous cellular tissue. The extreme mobility of the separate organs and parts of organs is mainly owing to the same cause; and in every part of the body in which greater or less deposits of fat are met with, nature appears to have had a similar object in view. Hence fat is found to remain the longest in the parts where it is most needed, as in the heart and in the orbit of the eye. How could so complicated a muscular structure as the heart move with freedom, ease, and regularity, if the interstices formed by the muscular bundles often contracting in opposite directions were not filled with fat, and if the vessels proceeding from them were not completely enclosed in fat? How would the muscles of the eye, and indeed the eye itself, act, if we could remove all the fat from the orbit of the living subject? Deprived of this protection, the muscles would become unable to discharge their functions, the optic nerve would be compressed, and sight utterly destroyed. Thus, too, we find in the rounded abdominal cavity, which is traversed by the cylindrical intestinal canal, that every fissure and interstice is filled up with fatty masses; in the great omentum, in the mesentery, and the *appendices epiploicæ*,—wherever there is an interstice—we find fat; and it is most evident, that by these means all friction, and every violent shock, are diminished, while a free peristaltic movement is afforded to the intestinal canal. The lower part of the pelvis is especially furnished with fat of so yielding a nature as to permit of the organs of excretion contained in it, being dilated at will. How different would be the appearance of the face if all the fat were removed from the muscles and from below the skin! The fat which smooths the bony corners and angles, and the narrow muscles of the face, is the cosmetic employed by nature to stamp the human countenance with the incomparable impress which exalts it far above all the lower animals. A similar physical use seems to be equally apparent in the deposition of fat on the extremities, although its presence may there be subservient to other purposes.

Although we find but little fat in the extremities of persons who are accustomed to exercise their muscles strongly, the quantity present is yet sufficient to effect the purposes already indicated.

Fat, when in a fluid state, is moreover a very *bad conductor of heat*. This property of fat has been most wonderfully employed by nature for the protection of the animal body from the injurious effects of excessive heat or cold, and of rapid alternations of temperature. Every one acquainted with the propagation of heat in fluid bodies, will easily perceive, that by the distribution of fat in small cells and layers, by which the rising and falling of the heated or cooled fluid is impeded, nature has most perfectly effected the object in view. We surround our stoves with stagnant air, in order to retain the heat as much as possible; but this object would be far more perfectly attained, if we could enclose the air in the subjacent and superimposed layers of so bad a conducting medium as the cellular tissue. When we consider the enormous quantity of cells filled with fat which are frequently deposited under the skin of corpulent persons, we can scarcely comprehend how an otherwise healthy individual could die from the effects of excessive cold.

Thus we find that the whole abdomen is filled and covered with fat, for the purpose of maintaining that equable temperature which is requisite for the due performance of its various chemico-physiological processes, the adipose tissue of the omentum acting as a special protection to the abdominal viscera. In furtherance of a similar end, the female breasts are largely supplied with fat, since, from their exposed position, these organs might, without such a protection, readily become unfitted for their normal functions. The testicles, on the other hand, contain no fat, and the scrotum very little, because these organs must be kept cool, as we learn from the bad results following the non-descent of the testicles. Animal heat could not be maintained in so equable a condition in the body, if all the organs—every part in which a metamorphosis of tissue occurs—were not enveloped in fat. Do we not observe how eagerly phthisical patients, convalescents, and old persons, seek the warmth of the sun, and how emaciated animals delight in basking in its rays? We should probably also take into consideration the fact that, next to water, fat possesses the greatest capacity for heat, and hence a very considerable quantity of heat will be required to transmit warmth through the fatty investment of the body. As a proof that fat possesses these useful properties, we may refer to the practice common alike to the nations of the extreme north, and to the inhabitants of many tropical lands, of anointing the skin with fat, in order to guard in the one case against intense cold, and in the other against extreme heat.

The various uses arising from the low *specific gravity* of fat scarcely require comment. It would be almost impossible to swim without fat, and although it might be advanced that swimming is not a necessary faculty of the human body, we shall readily be disposed to admit the utility of fat in this respect when we consider that, if the muscles of only an arm were encompassed with pure water instead of fat, the force of the muscles, which is, moreover, better adapted to rapid movement than to overcome a resisting power, would undoubtedly be very considerably diminished; for there can be no doubt that in *hydrops anasarca* the muscular weakness does not depend alone on the tension, and on the morbid diminution of the muscular activity, but likewise on the altered condition of gravity of the whole extremity, depending on the accumulation of water and diminution of fat.

One of the best known properties of fat, is that of its rendering other bodies *supple*, and diminishing as much as possible the brittleness of bodies, and the friction of parts moving on one another. This use is made most apparent in the movement of the muscles, and the free action of the joints. In this point of view, the utility of fat is nowhere more conspicuous than in the bones. Fat, undoubtedly, gives great flexibility to the earthy bones, as we perceive from their brittleness when macerated; and as is made most apparent in the disease of the bones inaptly termed osteomalacia, for, while there is so extraordinary a loss of osseous matter, that the bones appear, when macerated, to consist of a mere gauze-like tissue, most of the interstices are entirely filled with fat, as if the *vis naturæ medicatrix* would in some degree compensate, by an excessive accumulation of fat, for that property of the bones which has been destroyed by this disease.

I found, in the ribs of a patient who had died in a state of extreme osteomalacia, 56·92% of fat together with 24·665% of other organic matters, 15·881% of phosphate, and 2·534% of carbonate of lime.

The utility of fat, considered in a mechanical point of view, is so evident from what has been already said, that it would seem superfluous to add any further remarks on the subject. If negative evidence were admissible, we might observe that fatty deposits are rarely or never found in the brain and lungs, where their presence would occasion mechanical injury, since external pressure, and even a slight increase of heat, would prove injurious to these organs. In the *glans penis* again we find no fat, because its presence would, undoubtedly, contribute to increase the irritability of this organ.

Before we proceed to the consideration of the chemico-physical uses of fat, we will cursorily advert to the view which has long prevailed in physiology, that the fat deposited in the areolar tissue is nothing more than a stored-up nutriment. This proposition, advanced in accordance with the earlier views of natural philosophy, appeared to derive a considerable degree of corroboration from a general consideration of the fatness and leanness of men and animals, under different physiological or pathological relations; but such a method of observation is too vague and general any longer to maintain its ground in the present position of science. We have ceased to believe in the existence of a special administrator of the economy of the living organism, who, under the title of *vital force*, prepares, in times of plenty, for a season of scarcity; and we now know that the process of the deposition of fat in the areolar tissue is not so simple, and that its resorption does not admit of so ready a solution as was, at one time, believed to be the case. Thus, it must not be supposed that fat simply collects in the interstices of the cellular tissue, from which it may be as easily removed as the water which occasionally accumulates therein in *hydrops anasarca*. Fat is not contained in a free state within the interstices of the areolar tissue, but is contained in special cells, enclosed by an albuminous wall, and provided originally with a nucleus, the so-called cytoblast. Fat, therefore, only collects in the cellular tissue by means of a cell-formation, and hence it is, in many cases, extremely difficult to explain how fat can so rapidly disappear from the areolar tissue. It has not even been clearly determined whether the whole cell is resorbed with the fat, or whether, as Gurlt* maintains, the cell remains, and is filled with serum instead of fat. We must remember, in considering the observations made on the increase or diminution of fat in men and animals in a healthy as well as a diseased condition, that fat-cells, like most other animal cells, stand in a constantly alternating relation to the other fluids, more especially the blood. The constitution of the blood is reflected in all parts of the animal body, and endosmotic and counter currents must be established as soon as one of the fluids in question is subjected to any alteration. It is not necessary that we should assume with Mascagni that each fat-cell is provided with an artery and a vein, for the relations of endosmosis with which we are at present acquainted sufficiently explain the different results of this mutual action between the nutrient fluid and the fat-cell. In rapid emaciation, and more particularly in those conditions of the body which are usually termed anæmic, (as, for instance, after repeated blood-letting and other losses of the animal fluids, and after typhus and other severe diseases,) fat is often accumulated in the blood, while it disappears from the sub-cutaneous cellular tissue. Conversely, the formation of fat-cells often appears to be more rapid than the reproduction of other tissues after anæmic conditions, when the blood has not quite recovered its normal character; hence we frequently observe a very abundant deposition of fat after typhus and other diseases resulting in anæmia. We shall enter more fully into the consideration of this subject, when we proceed, at the close of the physiological chemistry, to treat of the general phenomena of nutrition.

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* Physiol. S. 20.

We now enter upon what may be termed the physico-physiological uses of fats. Liebig has shown, with his characteristic ingenuity, that the fats mainly contribute to *the excitement and maintenance of animal heat.* One of the most ingenious of Liebig's deductions is his classification of the elements of nutrition into true plastic nutrient substances and food for the respiration, to the latter of which he especially ascribes the functions of maintaining animal heat. But as, in our observations on the processes of respiration and nutrition (in the third volume), we shall enter more fully into the examination of Liebig's views on this subject, we shall here only observe that, however paradoxical and apodictic many of his deductions may appear, he has founded a new era in physiological chemistry, and has been the means of throwing a clearer light over the whole economy of the organism. Owing to his aphoristic mode of representation, his views have often been misunderstood and erroneously interpreted, and many persons have even supposed that they must assume that fat is simply transferred into the blood, where it is burned like the oil in a lamp, or the coke in a steam-engine. A more attentive examination of Liebig's writings shows, however, that he did not entertain so crude a view of the subject. But we must admit that we do not consider as wholly groundless the objection which has been advanced against Liebig, that he regards animal heat as too independent of other processes. Animal heat can only be considered under one of two points of view; that of being an incidental phenomenon and the mere result of certain vital processes, or as being necessary to the maintenance of definite animal processes and functions. If the latter view be even partially correct, we must recollect that animal life is not generally dependent upon a definite high temperature, and that numerous cold-blooded vertebrate animals perform the processes of digestion, respiration, blood-formation, and of the nervous system, as well at a low temperature, as warm-blooded animals do at 37°·5. If, on the other hand, animal heat were a mere incidental phenomenon, the fats would appear to be most uselessly expended in serving no other purpose than that of developing heat. The fat of the living body therefore probably conduces to other ends in the animal economy.

I was long since led, from theoretical grounds, to regard the fat as one of the *most active agents in the metamorphosis of animal matter*; and this subjective conviction has since been converted into objective proof by numerous experiments and observations. After having found by experiments regarding the fermentation of milk,* that this process cannot be excited by albuminous bodies in saccharine or amylaceous fluids, excepting with the coöperation of fat, I next ascertained that a certain, although small quantity of fat, was indispensable to the metamorphosis and solution of nitrogenous articles of food during the process of gastric digestion. Elsässer† has confirmed the fact by the observation that, in experiments on artificial digestion, the solution of articles used as food is considerably accelerated by means of fat. It is easy to ascertain by means of artificial openings in the stomachs of dogs, that flesh containing only little fat, and especially albuminous substances which have been designedly deprived of their fat, remain longer in the stomach, and therefore require a longer period for their metamorphosis, than the same substances when mixed or impregnated with a little fat. An excess of fat appears, on the other hand, at least in persons of weak digestion, to exert an injurious action. The pancreatic juice most probably owes a portion of its utility in promoting digestion to the quantity of fat which it contains.

The pancreatic juice, like pus, deposits, according to Cl. Bernard,‡ fine crystalline bundles of margarin and margaric acid during its spontaneous decomposition at a high temperature.

Although we are unable fully to demonstrate the special agency of fat in the further metamorphosis of the digested food, namely, in the formation of chyle and blood, yet we need only observe the intestinal villi during the process of digestion, and see their individual cells filled either with clear fat or dilated by a grumous matter—we need only institute a microscopic and chemical comparison of the fat in the chyle found in the finest lacteals with the contents of the thoracic duct, in relation to the different quantity and character of the fat in both fluids—in order to perceive that fat is not only resorbed, but that it also influences the metamorphosis of the albuminous constituents of the nutrient fluid. Is it probable that fat would so tenaciously adhere, even under different modifications, to some of the constituents of the blood, unless it exercised some influence on their origin or metamorphosis? Or are we to suppose that the fat, which we can extract from the animal nerves by boiling them with alcohol, or digesting them with ether, and whose removal leaves the separate nerve-fibres like hollow cylinders with thick walls, is deposited there for no useful end, and that it can be wholly free from all coöperation in the function of the nervous system?

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* Simon's Beiträge. Bd. 1, S. 63-77.

† Magenerweichung der Kinder. S. 112.

‡ Arch. gén. de Méd. 4 Sér. T. 19, p. 71.

However opposed we may be to teleological explanations, we cannot deny the importance of an enquiry into the grounds and aims of obscure subjects, since it is by such means that natural enquiry has ever been guided into those paths which lead to the investigation of causes, and the final comprehension of phenomena.

We have already become acquainted with two species of animal cells, in which fat is the main constituent, viz., true fat-cells and certain kinds of granular cells (the so-called inflammatory globules) found in milk, (Corps granuleux, Colostrum-corpuscles,) in the sputa in chronic catarrh, in old apoplectic cysts, &c. Fat, however, would appear from some of the latest investigations of the most distinguished physiologists, to play a very important part in every kind of cell-development; indeed most enquirers agree in regarding it as affording the primary foundation in the formation of a cell. Acherson[*] was undoubtedly the first to direct attention to this subject by his discovery that albumen always coagulates around a fat-globule placed in an albuminous solution; and although the question may not be so simple as Acherson would make it appear, the presence of fat in the cell during its formation, and its importance in affording the predisposing cause of cellular formation, is no longer denied by any physiologist, whether he adhere to the old theory of cell-development established by Schwann and maintained by Kölliker, or advocate the views of Henle, or of Reichert. According to Hünefeld, Nasse, and others, the nucleoli invariably consist of fat. The newly secreted or recently formed plasma always contains more free fat than after the nuclei or cells have been deposited,—a fact that is clearly demonstrated in H. Müller's[†] excellent memoir on the chyle and its histological elements, who shows that the cloudy turbidity of the chyle which depends on the presence of the fat, disappears in proportion as the isolated granules, the aggregated granules, and the cells are developed. The serum of pus moreover contains much less fat than pus-corpuscles. In the blood we find that fat is especially deposited in the cells and in the fibrin, the granular contents of many of the blood-corpuscles consisting of this substance. All plastic exudations contain more fat than the non-plastic; for the latter, as dropsical fluids and tubercular masses, although occasionally containing much cholesterin, usually contain very little true fat; while on the other hand exuberant, highly cellular cancers abound in this ingredient.

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[*] Müller's Arch. 1840. S. 49. [In connexion with this subject, I may refer to a Memoir on "the Structural Relation of oil and albumen in the animal economy," read by Professor Bennett before the Royal Society of Edinburgh, and published in the "Monthly Journal of Medical Science," Vol. 8, p. 166; a Lecture published by myself in the "London Medical Gazette," for May, 1848, New Series, vol. 6, p. 140; and v. Wittich, Ueber die Hymenogonie des Eiweisses. Königsberg, 1850.—G. E. D.]

[†] Zeitschr. f. rat. Med. Bd. 2, S. 233.

In pus, the pus-corpuscles often sink some lines below the level of the fluid; on comparing the amount of fat in the supernatant serum with that in the pus beneath it in which the corpuscles were suspended, I observed, in two experiments conducted with different pus, that in one there was only 7·13% of fat in the solid residue of the serum (which should have contained most of the fat since it was taken from the surface of the pus after it had stood a long time,) while the thick purulent sediment contained 18·41%; in the other case there was 9·084% in the residue of the serum, and 17·14% in that of the pus. The difference between the amount of fat in the serum of the pus and in the pus-corpuscles is most plainly apparent when both the sediment and the serum of good pus are suffered to remain in well closed vessels. Both fluids become acid, and fats and fatty acids are separated from them; in the former these changes are but slightly developed, whilst the acid purulent sediment exhibits, under the microscope, an innumerable quantity of the most beautiful crystallisations of margaric acid and of margarin, with cholesterin.

The fats of the blood are also principally deposited in the cells or blood-corpuscles. I found in 100 parts of well dried blood-corpuscles taken from the blood of the ox, and whose mode of preparation I shall explain in the second volume of this work, 2·214% of fat in one experiment, and 2·284% in another; the fibrin of the same blood contained in the one instance 3·218%, in the other 3·189% of fat; while 100 parts of the solid residue of the serum yielded 1·821, and 1·791 parts of fat. The blood-corpuscles have, unfortunately, scarcely ever been examined with reference to their amount of fat; in other respects, however, a comparison with the analyses instituted by other observers on the blood, leads to the same result.

It may be observed, in reference to the small quantity of fat contained in tubercles, that many fat-vesicles are often discovered under the microscope in recent tubercular deposits, as, for instance, in gelatinous tubercles, but that gray, solid tubercles, when submitted to a chemical analysis, after the separation of the cholesterin, which although not belonging to the fats is always reckoned amongst them, are found to contain very little fat. In a gray tubercular mass, I once discovered only 3·54§ in the well-dried substance, although almost every other tissue contained far more fat. Becquerel and Rodier* found, moreover, that in tuberculosis the saponified fats were far more diminished in the blood than in any other fluid.

We may here, perhaps, find some explanation of the mode of action of cod-liver oil, whose utility cannot be wholly denied even by that spirit of scepticism which has of late been so prevalent in medicine; and we have always been of opinion that cod-liver oil acts upon certain stages of disease more by its true fatty nature than by the small quantity of iodine which it contains. In confirmation of this view we may observe that many experienced practitioners (Oppolzer among the number) have found that almond oil and other similar oils are as efficacious as the loathsome cod-liver oil. But the idea that cod-liver oil, considered (according to the misconception of Liebig's views†) as a mere material of combustion, should be of benefit in a disease where the lungs are so entirely clogged or degenerated that an extensive oxidation of the blood is impossible, can only be entertained by persons wholly ignorant of the character of tuberculosis or of pulmonary consumption. No chemical analysis is needed to show that cellular cancer (encephaloid) and sarcoma abound in fat, and every one who has examined one or two of such tumours microscopically will be able to confirm the truth of this ordinary observation.

When we consider all these facts we shall be almost involuntarily led to the conclusion that fat takes a highly important share in the most important, and at the same time the most mysterious processes in the formation of cells and tissues. We cannot believe that fat is a mere incidental agent in all these processes, but we must rather regard it as of essential aid in the process of converting nitrogenous nutrient substances into cells and masses of fibres, in like manner as it coöperates in the processes of lactic fermentation and digestion; and it is probable that whenever a chemical equation representing the formation and function of certain cells can be established, fat will constitute one of the integral factors. Indeed it is impossible to believe that in the vital activity of cellular action, fat should be without influence on the metamorphosis of the substances which it accompanies, and that without reference to them, it should obey only its own affinities towards oxygen or an alkali.

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* Gaz. méd. 1844. No. 51.

† Ann. d. Ch. u. Pharm. Bd. 58, S. 84-89.

In considering fat as an important agent in the various phases of the metamorphosis of animal matter, we cannot, however, refer its action solely to mere contact or a catalytic force, but we are constrained to assume that it coöperates in the metamorphic action, and experiences metamorphoses, combinations, and decompositions. None but those chemists, who, imagining they comprehend Liebig's views, have framed and illustrated a physiology of their own, in the same manner as speculative natural philosophers have attempted *à priori* to construct the laws of the natural sciences, could have regarded the animal body as a furnace, and fat as a simple and crude material of combustion. It is, however, the province of physiological chemistry to trace the chemical phenomena of the animal body and its various substances in their separate phases of metamorphosis, and from the knowledge thus obtained, to sketch the grand and universal features of chemical action in the living body. It would be equally unphysiological and unscientific to suppose that the requirements of physiology would be fully satisfied by our proving that fat becomes finally decomposed into carbonic acid and water. The province of physiological chemistry is rather to show whether fat, or rather the fatty acids, always gradually and successively lose two atoms of carbo-hydrogen, that is to say, whether remaining in accordance with the general formula, they become converted into acids of the first group, and are then finally decomposed into carbonic acid water; or whether fats contribute by their metamorphosis in the animal body to form other known animal substances. As, however, in the present state of our positive knowledge, we are unfortunately not in a position to answer this question with certainty, it is better to confess our ignorance, than to indulge in vague conjecture, although many chemical and physiological experiments afford some support to the hypothesis, that the fats take a part in the formation of other substances which cannot be regarded as mere products of their oxidation.

Since we find so large a quantity of saponified fats in the blood and other animal fluids, as for instance in the bile, it is not improbable that the first step in the alteration of the fats consists in their decomposition into glycerine and the corresponding fatty acids.

If we assume that the fats are subjected to so gradual an oxidation that their carbo-hydrogen radical gradually diminishes by 2 atoms of carbo-hydrogen, it is singular that we should find the fatty acids which mark the gradations from capric to margaric acid in plants, but not in animals; for while the formation of fatty acids with a high atomic weight is very gradual in plants, a similar law does not prevail in reference to their regressive formation in animals, for here we meet with no acids besides margaric and stearic having a fat-radical of the formula, C_nH_{n-1}. It would appear, therefore, that the fatty acids, when separated from glycerine (to which reference has already been made at p. 243) enter into complicated combinations and metamorphoses, in which it is not easy to recognise or detect their presence. We have already (at p. 126) noticed the probability that the principal acid contained in the bile, cholic acid, is a conjugated fatty acid; chemical experiments giving evidence of the presence of oleic acid in it, although it cannot actually be separated.

The hypothesis, that *a portion of the fat takes part in the formation of bile,* is further confirmed by numerous physiological and pathological experiments.

The following physiological facts in some degree confirm this view. A close observation of the development of the chick within the egg, leads us almost irresistibly to the opinion, that towards the close of the period of incubation, a portion of the fat in the yolk-sac (when it is drawn into the abdominal cavity and adheres to the liver) is converted into biliary matter; and every physiological enquirer, who has occupied himself with this subject, must have observed the greenish tint which is often, although not always, very distinctly visible in the yolk-sac, and especially along the course of the veins. On one occasion I found this colour so intense, that I was induced to treat the whole of the yolk-sac and its contents with boiling alcohol, and examine it for bile, according to the method described at p. 123; when the ordinary bile-reaction was obtained by Pettenkofer's test. The veins of the yolk-sac pass into the liver, and it is well known that the vessels of the yolk-sac for the most part resorb the yolk, and transfer it into the liver; for the earlier view that the yolk passes through the *ductus vitello-intestinalis* into the intestine, and is carried from thence into the liver by the biliary ducts, is incorrect. The liver at this period serves mainly, as E. H. Weber,* and Kölliker† have shown, to form colourless and coloured blood-corpuscles, and not to produce or secrete bile, for I have frequently convinced myself by observations on human and animal embryos, that at this period the gall-bladder contains no bile.

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* Zeitschr. f. rat. Med. Bd. 4, S. 160-164.

† Ibid. Bd. 4, S. 112-160.

The *blood of the portal vein,* from which the bile is principally formed, differs from all other blood, whether venous or arterial, by its large quantity of fat, as was noticed by Simon and Schultz, and has been corroborated more recently by the exact quantitative analyses of Fr. Chr. Schmid,* who found that the blood of the portal vein contained so much more fat than that of the jugular vein, that he was led to regard this as the most essential difference between these two kinds of blood. Moreover he observed that the fat from the blood of the portal vein was of a dark brown colour, and that it was always richer in olein, and consequently more greasy, than the fat of other venous blood, which is white and crystalline. When animals are *starved* for any length of time it is well known that they rapidly become emaciated; the urine still exibits nitrogenous constituents, corresponding in amount to the products of effete tissue; whilst the gall-bladder is perfectly full, and the liver constantly pours forth bile into the intestine, as I have convinced myself by a repetition of Magendie's experiments.† The above fact seems to explain the cause of the bitter taste of which persons suffering from starvation very frequently complain. Whence can the liver extract the materials necessary to the formation of bile? The urine, although poorer in solid constituents, always contains a considerable quantity of urea; and the animal body contains few or no highly carbonaceous substances, with the exception of fat, which we here observe disappearing very rapidly, while at the same time there is an abundant secretion of bile.

In *disease* the diminution or increase of fat is inversely proportional to the secretion of bile. Polycholia, which seldom occurs in adults, but which in children constitutes the affection known as *Icterus neonatorum,* is always accompanied with rapid emaciation. In acute diseases, emaciation generally occurs in conjunction with critical symptoms, that is to say, when the organs of excretion resume their activity, and eliminate the materials that have become effete; hence the copious semi-solid fæces. In all acute or chronic diseases of the liver, the fat accumulates either merely in the blood, or in the blood and in the cellular tissue. The obesity observed in habitual drunkards is not in consequence of their taking too much combustible material into their bodies, (brandy drinkers moreover generally take only small quantities of solid food,) but in consequence of the disturbed hepatic action, which the invariably abormal condition of the liver, found in after death in these cases, proves to have existed.

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* Heller's Arch. Bd. 3, S. 487-521, and Bd. 4, S. 15-37, and S. 97-132.

† Journ. de Physiol. T. 8, p. 171.

Traill* and Lecanu have found the blood extremely rich in fat in inflammation of the liver; and Lassaigne,† and more recently Becquerel and Rodier, found the quantity of the fat in the blood more increased in icterus than in any other disease. Dobson, Rollo, and Marcet, observed so large a quantity of fat in the blood of diabetic patients that it resembled an emulsion; but I have myself only on two occasions found the blood to be largely charged with fat in diabetes, and here the disease was complicated with an affection of the liver, and the excrements of the patients were pale, and almost of a grayish-white tint.

All these facts render it difficult to deny the existence of a connexion between fat and the formation of bile.

It is not, however, wholly impossible that fat should contribute in some measure to the formation of other substances, but we will here simply observe that facts subsequently to be noticed give some probability to the opinion that fat likewise coöperates in the *formation of the blood-pigment.*

We trust that the above remarks will lead to a more careful enquiry into the metamorphoses and function of fat in the healthy and diseased body, and be the means of assigning a higher degree of importance to this substance, than has hitherto been awarded to it in the animal economy.

HYDRATED OXIDE OF CETYL.—$C_{32}H_{33}O.HO$.

Chemical Relations.

Properties.—This substance, to which its discoverer, Dumas, gave the name of *ethal*, forms white, solid, crystalline plates, melts at about 56°, again solidifies at 48°, and volatilises readily either alone or with aqueous vapour, when heated; it is devoid of smell and taste, is insoluble in water, but dissolves in all proportions in hot alcohol and ether, has no action on vegetable colours, and when ignited burns like wax. It is decomposed when heated with nitric acid;

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* Annals of Philos. 1823, vol. 5, p. 199.

† Journ. de Chim. méd. T. 2, p. 264.

heated to 220° with hydrated potash, it becomes converted (see p. 72,) into cetylic acid ($C_{32}H_{33}O+2HO+KO=4H+KO.C_{32}H_{31}O_3$). When warmed with concentrated sulphuric acid it forms an acid haloid salt.

Composition.—According to the above formula, deduced from the analyses of Dumas and Peligot,[*] this body consists of:

Carbon	32 atoms	....	79·339
Hydrogen	33 ,,	....	13·636
Oxygen	1 ,,	....	3.306
Water	1 ,,	....	3·719
			100·000

The atomic weight of the hypothetical anhydrous substance =2912·5.

This body, like glycerine, is the hydrate of a fatty base; but its composition and its relations of combination indicate that it is much more closely allied to the hydrated ethers or alcohols; in common with them it is included in the formula $C_nH_{n+1}O.HO$, it loses the one atom of water in combining with acids, and is converted by oxidation into an acid of the formula $C_nH_{n-1}O_3$. Oxide of cetyl or cetylic ether in an anhydrous state has not been obtained.

Combinations.—Very little is known of the *acid sulphate of oxide of cetyl* in its isolated state. Its combination with potash, which $= C_{32}H_{33}O.SO_3+KO.SO_3$ is obtained in minute, thin, nacreous plates.

Cetylate of oxide of cetyl, $C_{32}H_{33}O.C_{32}H_{31}O_3$ (Smith[†]) exists preformed, under the name of *cetin* or *spermaceti*, principally in the cavities of the skull, but also in the fat of other parts, of the *Physeter macrocephalus*. To obtain it in a state of purity, we must repeatedly crystallise it from hot spirit, of 0·816 specific gravity. It separates in minute, nacreous, white plates, devoid of smell and taste; it fuses at 49°, but on cooling solidifies in a crystalline form; it volatilises at 360° without decomposition, dissolves in 40 parts of boiling spirit, of 0·821 specific gravity, and more readily in anhydrous alcohol and ether; when submitted to dry distillation it yields no pyroleic acid, and when digested with nitric acid it yields adipic but no suberic acid. When heated with hydrated potash it is resolved into hydrated oxide of cetyl and cetylic acid.

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[*] Ann. d. Chim. et de Phys. T. 72, p. 5.

[†] Ann. d. Ch. u. Pharm. Bd. 42, S. 40-51.

Preparation.—In order to obtain hydrated oxide of cetyl, pulverised hydrated potash must be added to melted spermaceti, and the mixture be continuously stirred; when the mass has become solid it must be digested with water, and the soap which is thus produced must be treated with hot dilute hydrochloric acid; after the oily stratum has been again fused with caustic potash, and digested with hydrochloric acid in order to ensure the perfect decomposition of the cetin, the mixture of cetylic acid and oxide of cetyl must be digested with milk of lime and evaporated. From this mixture we can take up the hydrated oxide of cetyl by cold alcohol, which does not dissolve the cetylate of lime.

Tests.—It is impossible to recognise this substance with certainty unless by an elementary analysis.

Physiological Relations.

Hydrated oxide of cetyl has not yet been found in an isolated form; spermaceti, however, occurs in several parts of the Cachalot, mixed with ordinary fat; in greatest quantity, however, in the head, not in the actual cavity of the cranium, but in a large excavation on either side of the upper part of the head and lying external to the nostrils. Regarding the formation and uses of this substance, we can only offer the same opinions as respecting the fats in general.

The *doeglic oxide* of Scharling is too hypothetical a body to be entitled to be yet classed among the haloid bases. Compare p. 116.

Lipoids.

Under this head we place what are termed the non-saponifiable fats, that is to say, such bodies as have many physical properties in common with the salts of oxide of lipyl, but do not resemble them in their composition or in their products of decomposition, and consequently cannot be placed amongst the true fats. In this class we place ***cholesterin***, ***serolin***, ***castorin***, and ***ambrein***.

CHOLESTERIN.—$C_{37}H_{32}O$.

Chemical Relations.

Properties.—This body, formerly known as *biliary fat*, separates from its solutions in nacreous scales containing 2 atoms of water; examined under the microscope, these crystals appear in very thin rhombic tablets, whose obtuse angles = 100° 30′, and whose acute angles = 79° 30′; it fuses at 145°, solidifying again, and becoming perfectly crystalline at 135°; it may be distilled *in vacuo* at 360° without undergoing decomposition; it becomes electrical on friction, is perfectly insoluble in water, but dissolves in 9 parts of boiling alcohol, from which the greater part again separates on cooling; it is also slightly soluble in soap-water, and more freely in the fatty oils and taurocholic acid; it is inflammable, and burns with a smoky flame. Treated with concentrated sulphuric acid it assumes a red tint at 60°, and is converted, with the loss of water, into three probably polymeric carbo-hydrogens, which their discoverer, Zwenger,* has named *cholesterilins.* If cholesterin be heated with concentrated phosphoric acid to its melting point, there are formed two carbo-hydrogens, isomeric with the cholesterilins, to which Zwenger† has applied the name of *cholesterones.* By prolonged boiling with concentrated nitric acid, it becomes first converted into a resinous mass, which, by prolonged digestion, is resolved (Redtenbacher‡) into acetic, butyric, caproic, oxalic, and cholesteric acids (see page 122). A portion of the hydrogen may be abstracted from cholesterin by chlorine or bromine, of which an equivalent quantity takes the place of the hydrogen thus removed. It is not decomposed by concentrated alkalies, even when the mixture is submitted to prolonged heat. On dry distillation it leaves a charcoal, and yields an oily distillate, which after rectification with water evolves an agreeable odour, resembling that of the Geranium.

Composition.—Cholesterin has been analysed by Marchand,§ Schwendler and Meissner, and subsequently by Payen,‖ with tolerably similar results, which have led to the establishment of the above formula, $C_{37}H_{32}O$. As we have not yet succeeded in combining cholesterin with any other body, we have no means of controlling this formula and of determining its atomic weight. Zwenger has very recently analysed the *cholesterilins*, of which he was the discoverer, and found them composed in a tolerably uniform manner. He assumes, however, that there are differences between them, and that they may be respectively represented by $C_{32}H_{26}$, $C_{22}H_{18}$, and $C_{27}H_{22}$; and he believes that cholesterin consists of these three carbo-hydrogens and 3 atoms of water, its formula being, according to his views, $C_{81}H_{69}O_3$. Taking into consideration the limited accuracy which we are capable of attaining in our elementary analyses, and the method by which we deduce a formula from empirical results, we must regard Zwenger's view as, at present, very hypothetical.

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* Ann. d. Ch. u. Pharm. Bd. 66, S. 5-13.

† Ibid. Bd. 69, S. 347-354.

‡ Ibid. Bd. 57, S. 162-170.

§ Journ. f. pr. Ch. Bd. 16, S. 37-48.

‖ Ann. de Chim. et de Phys. 3 Sér. T. 1, p. 54.

We give the composition of cholesterin according to both formulæ:

Carbon	37 atoms	84·733	81 atoms	83·93
Hydrogen	32 „	12·214	69 „	11.91
Oxygen	1 „	3·053	3 „	4·16
		100·000		100·00

Notwithstanding its extraordinarily high numbers, Zwenger's formula accords more closely than the simpler one with the empirical results.

Products of decomposition.—*a. Cholesterilin*, $C_{32}H_{26}$, is earthy, amorphous, insoluble in water, and slightly soluble in alcohol; it differs from the two other carbo-hydrogens by its insolubility in ether; it crystallises from a hot oil of turpentine solution, and melts and is decomposed at 240°.

b. Cholesterilin, $C_{22}H_{18}$, crystallises in minute, strongly glistening plates or delicate needles, which are insoluble in water and alcohol, but soluble in ether; it fuses at 255°, and on cooling solidifies in a crystalline form.

c. Cholesterilin, $C_{27}H_{22}$, is a yellow, amorphous, resinous mass, freely soluble in ether, slightly so in alcohol, and insoluble in water; it fuses at 127°. Both this and the preceding variety are decomposed by heat. The formulæ must be regarded as entirely hypothetical, since the per-centage composition, both as found and as calculated, approximates to 88% of carbon, and 12% of hydrogen for all three of them.

a. Cholesterone is obtained by extracting with spirit the residue of cholesterin, heated with phosphoric acid to 137°; it crystallises in right rhombic, bilaterally acuminated prisms; is colourless, transparent, very lustrous, lighter than water, and melts at 68° into a colourless fluid, which very slowly reassumes the solid form; it can be distilled for the most part undecomposed, and burns with a smoky flame. It is insoluble in water, but dissolves freely in alcohol and ether, and in the volatile and fatty oils.

b. Cholesterone is extracted by ether from the residue insoluble in alcohol; it occurs in fine white needles, melts at 175°, cannot be distilled without partial decomposition, is lighter than water, is devoid of taste and smell, and burns with a smoky flame. Both varieties of cholesterone are devoid of oxygen, but contain about 12 parts hydrogen to 88 of carbon.

Preparation.—The best method of preparing cholesterin is by boiling gall-stones, containing this substance, with alcohol, and filtering the solution while hot; by recrystallisation from hot alcohol it is easily obtained in a state of purity.

Tests.—The recognition of cholesterin in the animal fluids is by no means so easy as might be supposed from the distinctive characters of this body; if, however, it has been once separated in a crystalline form, nothing is easier than to diagnose its presence with certainty. If, by its insolubility in water, acids, and alkalies, and by its solubility in alcohol and ether, it has been recognised as a fatty substance, it may be readily distinguished from all other similar substances by a measurement of the angles of the rhomb. It is only necessary to remark that the tablets are often so thin that their contour may be easily overlooked in a microscopic examination, if other morphological substances are simultaneously present in the field of the microscope: we must then slightly shade the field by a lateral or central diaphragm to make the outline stand forth more distinctly. In all this there is no difficulty; but it is, on the other hand, often very troublesome to obtain this substance in a crystalline form from oily fluids containing bile, or from soapy solutions. If we saponify with an alkali the fat which holds the cholesterin in solution, it also dissolves in the soap-water, and on the addition of an acid is again converted into the fatty acid; hence, when dealing with very small quantities of cholesterin, it is necessary to combine the fatty acid with oxide of lead, and to extract with boiling alcohol; the small quantity of dissolved margarate of lead is usually deposited previously to the separation of the cholesterin, which frequently does not crystallise, so as to be recognised by the microscope, until the fluid has been submitted to evaporation.

Physiological Relations.

Occurrence.—Small quantities occur in most of the animal fluids. It was originally discovered by Gren in *biliary calculi*, and has since been recognised as a constant ingredient of the *bile*. In the normal condition cholesterin is dissolved in the bile, and hence cannot be recognised under the microscope; even in the bile removed from the dead body we rarely find tablets of cholesterin (Gorup-Besanez*) and in these cases we cannot tell whether it depends on an augmentation of the cholesterin or on its separation in consequence of the decomposition of taurocholic acid. Frerichs† found no cholesterin in several examinations which he made of the bile in cases of fatty liver.

Cholesterin was first distinctly recognised as a normal constituent of the *blood* by Lecanu, Denis, Boudet, and Marchand; while Becquerel and Rodier‡ have especially directed attention to its augmentation and diminution in diseased conditions of the blood. According to these authors the amount of cholesterin in 1000 parts of normal blood ranges from 0·025 to 0·200 (the mean being 0·088). There is an augmentation of the cholesterin in the blood in old age, and in most acute diseases soon after the occurrence of febrile symptoms, especially in inflammations and in icterus. They have not discovered any physiological or pathological condition in which there is a constant diminution of this substance.

Cholesterin always occurs in the *brain*, where it was first discovered by Couërbe. Many subsequent observers have confirmed his observations.

It also appears to be an integral constituent of *pus*; at least whenever I have allowed pus to become sour I have found tablets of cholesterin in the decomposed mass; moreover, Caventou, Güterbock, Valentin, and many others have detected it in fresh pus.

Cholesterin is also very frequently found in dropsical exudations, especially in cysts; I have recently, on two occasions, analysed the *fluid of hydrocele* discharged by incision; both specimens were semi-solid rather than fluid, and when stirred, formed beautiful glistening bands. Their only morphological element was cholesterin.

Obsolete (*chalky*) *tubercle*, old *echinococcus-cysts*, such as are often found in the liver, and degenerated *ovaries* and *testicles*, often contain a large amount of cholesterin.

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* Untersuchungen üb. Galle. Erlangen, 1846. S. 58.

† Hannov. Ann. Bd. 5, H. I.

‡ Gaz. méd. 1844, No. 47.

I once found the *choroid Plexus* in the brain perfectly encrusted with cholesterin.

In *encysted tumours*, (especially in meliceris) as well as in *carcinomatous* and *other tumours*, we often meet with cholesterin.

In the *solid excrements* we may generally recognise traces of cholesterin; and in the *meconium* this substance is present in very considerable quantity.

In *pulmonary expectoration* I have only found cholesterin in the cheesy concretions ejected in advanced phthisis, and when vomicæ are already present.

In the *urine*, as far as I know, no cholesterin has yet been found.

[Möller states that he has twice discovered cholesterin in the pellicle which forms on the urine during pregnancy, but I know nothing of his character as an observer. See Casper's Wochenschr. 1845, N. 2, 3; or my translation of Simon's Animal Chemistry, vol. 2, p. 333. G. E. D.]

Origin.—In regard to the origin of cholesterin, which is never found in the vegetable kingdom but only in the animal body, we cannot offer even a probable conjecture. Judging from the mode of its occurrence, we must regard it as a product of decomposition; but from what substances and by what processes it is formed, it is impossible even to guess. Notwithstanding the similarity which many of its physical properties present to those of the fats, we can hardly suppose that it takes its origin from them, since the fats, for the most part, become oxidised in the animal body, whereas in order to form cholesterin, they must undergo a process of de-oxidation.

SEROLIN.

This body, which as yet has been very little studied, was discovered by Boudet,[*] in the solid residue of the serum of the blood.

At an ordinary temperature it appears in nacreous, glistening flocculi, which are very slightly soluble in cold, but dissolve pretty freely in hot alcohol, and in ether, and do not form an emulsion with water. This body has no reaction on vegetable colours, melts at +36°, and apparently may be distilled with only partial change.

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[*] Ann. de Chim. et de Phys. T. 52, p. 337.

The ammoniacal vapours and the very peculiar smell which it developes during distillation indicate that it contains nitrogen. It is not saponified by the alkalies.

Serolin is obtained by extracting, with hot alcohol, blood which has been dried, then boiled with water, and again dried. As the alcohol cools the serolin separates in flocculi.

CASTORIN.

This body occurs in *castoreum;* it crystallises from boiling alcoholic solutions in small, four-sided needles, is pulverisable when dried, melts at a temperature exceeding 100°, is not saponifiable, and is converted by concentrated nitric acid into nitrogenous, crystallisable, *castoric-acid.*

AMBREIN.

Ambrein is the principal constituent of amber; it crystallises in white needles grouped in stars or wart-like shapes, melts at 37°, cannot be saponified, and is converted by nitric acid into *ambreic acid,* $C_{21}H_{18}N_5O_3$, which is crystallisable, and forms yellow salts.

NON-NITROGENOUS NEUTRAL BODIES.

Most of the substances belonging to this class closely resemble one another in their empirical composition, and hence some of them have received the name of "carbo-hydrates"; for most of them contain hydrogen and oxygen in the same ratio as these elements are contained in water, so that if we suppose that they were combined into water, carbon would be the only remaining element of these bodies; indeed, even the number of atoms of carbon in them appears to be in accordance with a general rule, since in all the formulæ which as yet have been well established it is divisible by 6.

Considering their extremely analogous composition, it is naturally to be expected that these bodies should present many chemical properties in common with one another, various as their physical characters may be. They are so indifferent that it is only with few other bodies, and in these cases with considerable difficulty, that they can be made to combine, and then they enter into combination in multiple proportions, so that it is always difficult to determine their atomic weights with any degree of certainty. Almost the only physical properties which they have in common are deficiency in colour and smell. They are all decomposed by heat, and yield acid products of distillation. By digestion with dilute mineral acids, they are for the most part converted into glucose or grape-sugar. When decomposed by nitric acid, they yield oxalic acid, saccharic acid and mucic acid, and, perhaps, also, conjugated nitric acids. When treated with concentrated sulphuric acid these bodies become brown or black, and in addition to humin-like substances, form conjugated sulphuric acids.

The only substances of this group of any zoo-chemical importance are glucose or grape-sugar, milk-sugar, [inosite* or muscle-sugar] and cellulose.

GLUCOSE.—$C_{12}H_{12}O_{12}$.

Chemical Relations.

Properties.—Glucose, which is the name applied to grape-sugar by the French chemists, is identical with *diabetic sugar*, and crystallises with 2 atoms of water in wart-like masses consisting of minute plates arranged in a cauliflower form; these plates are rhombic and not square (as Saussure believed); when this substance separates rapidly from a solution, we may observe under the microscope that it occurs in irregularly striated, roundish masses, and not in plates; it is white, devoid of odour, and not so sweet as cane-sugar but sweeter than milk-sugar; it is only half as soluble in water as cane-sugar, but more soluble than milk-sugar; it is only slightly soluble in alcohol, and insoluble in ether; its aqueous solution turns the plane of polarisation of a ray of light to the right, and is devoid of action on vegetable colours.

At a few degrees below 100° it begins to cake together, but it melts perfectly at 100° with the loss of its 2 atoms of water; at 140° it becomes converted into caramel, and developes a sweetish odour; at a higher temperature it becomes frothy, grows brown, developes a pungent vapour, and leaves a voluminous charcoal.

In contact with nitrogenous bodies, and especially with casein, it undergoes the lactic, and subsequently the butyric fermentation; with common yeast it passes into the state of vinous fermentation. Digested with concentrated nitric acid, it developes nitric oxide gas, and is converted into oxalic and saccharic acids; while chlorine gas converts it into hydrochloric and saccharic acids. When digested with dilute sulphuric acid, its solution does not so rapidly become brown as that of cane-sugar, and it is only on evaporation that we observe the formation of a blackish brown residue; but its solution, when boiled with potash, very quickly assumes a fine brownish-red tint, and at the same time evolves a pungent, sweetish odour; it may be evaporated with lime-water without the development of any brown colour, the lime and the sugar forming a syrupy compound with a bitter taste. On treating an aqueous solution of glucose with caustic potash, and then adding a salt of oxide of copper, no precipitate is formed, but the solution assumes a beautiful azure tint: after some time, this gradually changes to a green colour, and finally a red powder is deposited; if the fluid be boiled, it at once assumes a yellow tint, and suboxide of copper is separated as a yellow or yellowish red powder. Glucose is distinguished by its property of forming a beautiful crystalline compound with chloride of sodium.

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* [Inosite or muscle-sugar has been discovered by Scherer since the original Publication of this volume. Its formula is $C_{12}H_{16}O_{16}$. It will be noticed in a future Part of this work. G. E. D.]

Composition.—According to the above formula, glucose consists of:

Carbon	.... 12 atoms	40·000
Hydrogen	.... 12 „	6·666
Oxygen	.... 12 „	53·334
		100·000

Its atomic weight=2250. (Peligot,* Erdmann and Lehmann.†)

Combinations.—The compound of *glucose and potash*, $2KO + C_{12}H_{12}O_{12}$, is obtained by adding an alcoholic solution of caustic potash to an alcoholic solution of glucose; it occurs in the form of white flocculi which, on exposure to the air, soon become tenacious and moist, and at length perfectly deliquescent; when dissolved in water they exhibit an alkaline reaction, and attract carbonic acid from the atmosphere.

The compound of *glucose and lime*, $2CaO + C_{12}H_{12}O_{12}$, is formed when a solution of glucose is mixed with an excess of lime, and the filtered fluid treated with alcohol; it forms a white mass, which on exposure to the atmosphere attracts water and becomes transparent.

It is not easy to obtain a combination of *glucose with oxide of*

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* Ann. de Ch. et de Phys. T. 66, p. 140, and Compt. rend. T. 6, p. 232.

† *Journ. f. pr. Ch.* Bd. 13, S. 113.

lead in definite proportions: its aqueous solution takes up a large quantity of this oxide; an insoluble compound is obtained from glucose and a solution of acetate of lead treated with ammonia.

The combination of *glucose with chloride of sodium*, $C_{12}H_{12}O_{12} + 2HO + C_{12}H_{12}O_{12}.NaCl$, may be obtained by the direct mixture of the solutions of the two constituents and by spontaneous evaporation, in very large, colourless, four-sided, double pyramids. These crystals are hard, easily pulverisable, of 1·5441 specific gravity, transparent, unaffected by the atmosphere, of a saline and sweetish taste, soluble in 3·685 parts of cold water, and difficult of solution in alcohol. At 100° the powdered crystals begin to cake together, and lose 4% of water; when rapidly heated to 120° they melt in their water of crystallisation, and begin to become brown at +160°. The crystals contain 13·3% of chloride of sodium.

Preparation.—This sugar is not only, as is well known, widely diffused throughout the vegetable kingdon, but may be formed from other kinds of sugar and from carbo-hydrates (starch, wood-fibre, &c.) by digestion with dilute acids; hence it may be prepared in many different ways. On the large scale it is commonly obtained from starch; but all that concerns us here is its mode of preparation from diabetic urine. The following is the ordinary mode of proceeding. Diabetic urine is treated with basic acetate of lead, and the excess of lead removed from the filtered fluid by sulphuretted hydrogen; the fluid is then evaporated, and extracted with alcohol, from which the sugar crystallises; but sugar thus obtained always contains acetates. In order to obtain the sugar I am in the habit of evaporating the urine to nearly the thickness of a syrup; provided it has not been too powerfully evaporated, the whole residue, after a variable time, becomes converted into a solid yellowish white mass, which must be extracted with absolute alcohol and subsequently with hot spirit. The sugar dissolved in the latter is removed, after it has crystallised, by filtration, while the spirit is submitted to evaporation, and then treated with a little water in order to facilitate further crystallisation. In this way we obtain the sugar in a state of greater purity than by the ordinary method.

In order to obtain diabetic sugar in a state of chemical purity, I prepared the chloride of sodium compound by saturating the aqueous solution of the alcoholic extract with chloride of sodium, and by repeated crystallisation obtained it in perfectly transparent crystals, which I dissolved in water, and cautiously precipitated with sulphate of silver; the fluid freed by filtration from the chloride of silver was evaporated, and the sugar was obtained in a state of chemical purity by extraction with alcohol; in order to remove any traces of this fluid, it must be recrystallised from distilled water.

Tests.—The methods of testing for sugar are not merely of importance in enabling the physician to establish his diagnosis in cases of diabetes mellitus, but likewise in consequence of the physiological relations of sugar to the general metamorphosis of tissue. Many chemists (amongst whom may be enumerated Golding Bird[*], Gairdner[†], Budge[‡], and myself,[§]) have turned their attention to the most accurate methods of discovering sugar. There has been much discussion regarding Trommer's[||] admirable test for sugar; but if this test be not admitted, equal objections may be advanced against all the reagents employed in mineral chemistry; for these also require to be used with proper care and circumspection; the application of most of them demanding more precaution and skilful manipulation than this test. It may be regarded as infallible for the recognition of the presence of sugar in diabetic urine; although a person utterly ignorant of chemical reagents may also here fall into error. In true Diabetes mellitus, the urine is free from those substances which may interfere with the reaction on which this test is founded, or rather with the judgment we form regarding this reaction; diabetic urine presents this difference from other saccharine urine, that the former with sulphate of copper and potash gives the reaction almost as readily as a pure solution of grape-sugar would do, even when there is but little sugar present, whilst the more normal urine in which sugar is a mere incidental constituent, gives a less distinct reaction; and the latter moreover precipitates other substances with the suboxide of copper, by which the colour of the precipitate is considerably modified.

The question here arises—what precautionary measures ought to be observed in the application of Trommer's test?

The fluid to be examined is treated with *caustic potash*, and filtered if necessary, that is to say, if there be too great a precipitate; an excess of caustic potash is productive of no harm, as it should be present in more than sufficient quantity to decompose the *sulphate of copper*; the latter, which must be added gradually, and in a diluted state, usually gives rise to a precipitate, which disappears when the fluid is stirred; as the quantity of the oxide of copper which is soluble is proportional to the quantity of sugar which is present, very little sulphate of copper must be added at a time, if we suspect that only a little sugar is present in the fluid. On allowing the azure solution thus obtained to stand for some time, there is usually formed a more pure red or yellow powder than the precipitate which is at once thrown down on boiling the fluid. Moreover, very prolonged heating is improper, for there are several substances which by prolonged boiling separate suboxide of copper from alkaline solutions of oxide of copper; amongst them we may especially name the albuminous substances, which with oxide of copper and potash yield very beautiful azure-blue, or somewhat violet solutions, and by very prolonged boiling, separate a little suboxide of copper, although without the aid of heat they have not this property.

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[*] Monthly Journal of Medical Science, vol. 4, p. 423, [and "Urinary Deposits," 3rd Ed. p. 352.—G. E. D.]

[†] Ibid. p. 564.

[‡] Arch. f. physiolog. Heilk. Bd. 3, S. 385.

[§] Schmidt's Jahrb. Bd. 45, S. 6-10.

[||] Ann. d. Ch. u. Pharm. Bd. 39, S. 360.

If a specimen of urine contain very little sugar, or if we are searching for sugar in some other fluid, it is advisable to extract the solid residue with alcohol, to dissolve the alcoholic extract in water, and to apply the potash and sulphate of copper to this solution. By proceding in this manner we usually obtain the reaction in its most distinct manner. If, however, we are seeking for very small quantities of sugar, as for instance in chyle, blood, or in the egg, we must neutralise the aqueous fluid, previously to its evaporation, with dilute acetic acid, in consequence of the solubility of albuminate of soda or of casein in alcohol, thus preventing any albuminous body from remaining in solution. If the reaction do not properly manifest itself in the alcoholic extract thus obtained, or if we would carry the investigation further, we must precipitate the sugar from the alcoholic solution by an alcoholic solution of potash, dissolve the compound of sugar and potash in water, and now apply the sulphate of copper; if only a trace of sugar be present, we obtain a most distinct and beautiful reaction.

The *fermentation-test* has been much extolled as a means of discovering sugar; but independently of the circumstance that the process is very tedious, it yields, to an inexperienced experimentalist and observer, far less certain results than Trommer's test. On adding yeast to a fluid, the phenomena of fermentation are simply dependent on the development of bubbles of carbonic acid; if this development of gas from a fluid, as, for instance, from diabetic urine, be not very active after the addition of yeast, we must not draw any conclusions regarding the presence of sugar, for yeast promotes the decomposition of the animal fluids—a process which is often accompanied with the development of a little gas. If, however, no yeast be added to the urine, but we wait for spontaneous fermentation, as has also been recommended, the development of carbonic acid proceeds very slowly, unless an extremely large quantity of sugar be present; moreover, in this case, there is this additional difficulty in observing the formation of the gas, that the sugar for the most part undergoes the lactic and not the vinous fermentation. As the detection of the alcohol, which is formed during this process, is by no means easy, attention has been drawn to the formation of the yeast-fungus (*Torula cerevisiæ*) as a characteristic indication of vinous fermentation. For those who are accustomed to the use of the microscope, and are well acquainted with the appearance of the *Torula*, this is unquestionably an easy and certain test; but it must be borne in mind, that when normal urine has been allowed to stand for a long time, especially at a high temperature, fungi of a precisely similar shape are formed in it, probably, for the most part, from the mucus. These fungi, which are by no means dependent on the decomposition of sugar, may exist in urine still preserving a decidedly acid reaction, although they more frequently occur in neutral urine; the individual cells, which, like the yeast-cells, (*Torula cerevisiæ*,) contain distinct nuclei, are mostly about one-half (in diameter) smaller than the true yeast-cells; but independently of the circumstance that under the microscope apparent magnitudes afford a very relative criterion, the yeast-cells which are first and spontaneously formed, are always much smaller than those which are subsequently produced by gemmation from previously formed yeast-fungi.

A very good means of discovering sugar, and of determining its quantity with considerable accuracy in a clear solution, is afforded by *Biot and Soleil's polarising apparatus;* its expense will, however, always stand in the way of its general application.

We have already shown (p. 124) that *Pettenkofer's test* is not available for the detection of sugar.

All other tests which were formerly employed for the discovery of sugar (evaporation with hydrochloric or sulphuric acid, treatment with chromic acid, boiling with caustic potash, &c.) are open to so many sources of fallacy, as compared with the methods we have already indicated, that we may pass them over in silence.

Trommer's test may also be successfully employed in the *quantitative determination* of the sugar in diabetic urine; Barreswil,[*] Falck,[†] and Scharlau,[‡] have recommended different methods of applying it with this view; the most generally applicable one, however, is that of Fehling.[§] As a test he uses a solution of 40 grammes of crystallised sulphate of copper in 160 grammes of water; this is mixed with a concentrated solution of 160 grammes of tartrate of potash and 560 grammes of a solution of caustic-soda (specific gravity=1·12), and water is then added till the volume of the fluid at +15° amounts to 1 litre. 11·5c.c. of a saccharine solution containing 5 grammes of dry sugar($=C_{12}H_{12}O_{12}$) in a litre, are necessary to cause the perfect reduction of the oxide to the suboxide of copper in 10c.c. of the test-fluid. Hence it follows that 100 parts of oxide of copper are completely reduced to the state of suboxide by 45·25 parts of sugar, or 10 atoms of oxide of copper by 1 atom of sugar. In order to determine with the greatest certainty the weight of the sugar from the volumetric measurement, and to render the errors of observation as small as possible, Fehling recommends that the urine to be examined for sugar should be diluted with water to 10 or 20 times its volume, that is to say, that 50 grammes of urine should be treated with 450 or 950 of water: 10 c.c. of the test-fluid are then to be diluted with about 40 c.c. of water, boiled, and so much of the diluted urine (which must be kept in a burette or graduated tube in order that we may be able to estimate the quantity used) added to it, as to effect as nearly as possible the complete decomposition of the sugar and of the oxide of copper. If any undecomposed oxide of copper be contained in the fluid after the removal of the suboxide by filtration, it may be recognised by the blue tint, and by its reaction with sulphuretted hydrogen: if, on the other hand, too much urine be added, the filtered fluid appears yellow from the action of the caustic alkali on the sugar. The point of thorough mutual decomposition is easily attained by a few repetitions of the experiment. As 10 c.c. of the test-fluid require 0·0577 of a gramme of sugar for the reduction of the oxide of copper contained in them, there must be exactly that amount of sugar in the quantity of urine used in the experiment, and hence the proportion of sugar in any given quantity of urine may be easily calculated.

Those who are not in the habit of using French weights and measures may prepare Fehling's test solution as follows:—Dissolve 69 grains of crystallised sulphate of copper in five times their weight of distilled water, and add to it, first, a concentrated solution of 268 grains of tartrate of potash, and then a solution of 80 grains of hydrate of soda in one ounce of distilled water. Put the solution into an alkalimeter tube, and add distilled water so as to make 1000 grain-measures of the liquor. This solution will be nearly double the strength of that made according to the above directions, and every 100 grain-measures of it will be equivalent to 1 grain of grape sugar. [G. E. D.]

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[*] Journ. de Pharm. T. 6, p. 301.

[†] Oesterlen's Jahrb. f. pr. Heilk. Bd. 1, S. 509.

[‡] Die Zuckerharnruhr. Berlin, 1846.

[§] Arch. f. phys. Heilk. Bd. 7, S. 64-73.

By *Soleil's polarising apparatus* the quantity of sugar may be determined with more rapidity than by the preceding method, and with equal accuracy. Many precautions are, however, requisite in its application, as has been especially shown by Dubrunfaut,[*] Clerget,[†] and Lespiau.[‡] We refer, therefore, to their communications on this subject; especially as Soleil's apparatus, in so far as its application to saccharine urine is concerned, is still deficient in many respects.

Fermentation was formerly employed to determine the quantity of sugar in fluids, the carbonic acid being determined, and the quantity of sugar calculated from it. This mode of determination is deficient in accuracy, in the first place, because all animal fluids, and especially the urine, contain free carbonic acid, and, secondly, because other constituents of the urine are simultaneously decomposed during the process of fermentation, and also yield carbonic acid. This method serves, however, very well for approximate and comparative determinations, if we allow a weighed quantity of diabetic urine to ferment at 37° in Fresenius's[†] alkalimetrical apparatus, and, as in alkalimetrical processes, determine the carbonic acid by the loss of weight.

This is the best means of determining the amount of sugar for ordinary medical purposes, Fehling's method being applicable rather to technology than to clinical medicine. If the apparatus be allowed to stand for about 48 hours at the above-mentioned temperature, all the sugar will have been converted into spirit; if we even omit to remove the carbonic acid by drawing a little air through the apparatus, previously to weighing, we shall still obtain results at all events sufficiently accurate for purposes of comparison.

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[*] Ann. d. Chim. et de Phys. 3 Sér. T. 18, p. 101.

[†] Compt. rend. T. 22, p. 200, and pp. 256-260.

[‡] Ibid. T. 26, p. 306.

[§] *Neue* Verfahrungsweisen zur Prüfung der Soda, &c. Heidelb. 1843.

Physiological Relations.

Occurrence.—In a *normal condition of the system* this form of sugar may always be recognised in the *primæ viæ*, especially in the *contents of the small intestine* after the use of vegetable, that is to say, of amylaceous and saccharine food. We shall subsequently see, when treating of digestion, that it is principally through the influence of the pancreatic juice that starch is gradually converted, in the intestinal canal, into sugar. It is only in small quantity that it exists in the contents of the small intestine, partly because the change effected in the starch proceeds very gradually, and partly because the sugar which is formed is very rapidly absorbed.

Trommer* was the first who detected traces of sugar in the *chyle;* I have several times most distinctly recognised the presence of sugar in the chyle of horses which, a few hours before they were killed, had taken either pure starch or strongly amylaceous food.

Sugar cannot generally be recognised in the *blood;* Magendie† however, asserts that he found considerable quantities of sugar, together with dextrin, in the blood of a dog, which for several days had been fed solely on boiled potatoes.

In a normal state it is probable that no sugar finds its way into the *urine;* at least after living for two days solely on fat and sugar, I was as unsuccessful in the search for sugar in my urine, as Magendie had been in the case of the dog in whose blood he found sugar.

It is only seldom that we meet with saccharine urine in *other diseases* than diabetes. Prout has sometimes found sugar in the urine of "gouty and dyspeptic persons," and Budge‡ in "abdominal affections and hypochondriasis." I§ once met with sugar in the urine of a puerperal woman, in whom, on the fifth day after delivery, the secretion of milk was suddenly suspended. I was led to the discovery that it contained sugar by observing the formation of yeast-cells in it; the sugar only continued in the urine of this woman for four days.

Although I have myself‖ once found sugar in the *saliva,* in a case of acute rheumatism, in which spontaneous salivation ensued, and this secretion was discharged in great abundance, I cannot venture to conclude from this isolated instance that sugar ever exists in the saliva of non-diabetic persons,, since in this case it is possible that the sugar might in some way have accidentally got into the vessel containing the saliva. So many heterogeneous substances find their way into the saliva, as we shall subsequently see, that there is nothing extravagant in the assumption that sugar may sometimes occur in morbid saliva. Wright places a sweet saliva amongst his numerous varieties; unfortunately, however, he did not proceed to ascertain whether the sweetness of this saliva was dependent on the presence of sugar, or whether it was a mere subjective sensation of the patient.

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* Ann. d. Ch. u. Pharm. Bd. 39, S. 360.

† Compt. rend. T. 30, p. 191-192.

‡ Arch. f. physiol. Heilk. Bd. 3, S. 413.

§ Jahresb. d. physiol. Ch. 1844, S. 27.

‖ Ibid. S. 20.

F. L. Winkler* found 8 grains of sugar in two softly-boiled eggs, which had been sat upon for some time, and whose white had a singularly sweet taste. I have recently convinced myself that small quantities of sugar are constantly present both in the *yolk* and in the *white* of fresh eggs.

I may remark that I experimented upon 30 eggs, in order to obtain evidence of the existence of small quantities of sugar. I have repeatedly, and with much care, repeated Winkler's experiment, in which he found so large a quantity of sugar (milk-sugar) in incubated eggs, but I cannot confirm his statement. I examined eggs that had been sat upon for 3, 7, and 15 days.

Bernard and Barreswil† have found sugar in the tissue of the liver even of animals that do not subsist on saccharine or amylaceous food.

[Experiments conducted in the Giessen laboratory have confirmed this statement, both in reference to the livers of graminivorous and carnivorous animals. See Liebig and Kopp's Annual Report, &c., for 1847-8, Vol. 2, p. 175, note 6.—G. E. D.]

At present I can only confirm this statement with reference to the liver of the frog; the extract obtained by cold alcohol from from frogs' livers was treated with double its volume of ether, in order to remove a portion of the biliary matters; the fluid decanted from the separated taurocholate of soda was treated with an alcoholic solution of potash. The great turbidity which was first induced was shortly replaced by a considerable precipitate of a resinous appearance, (the glucose and potash compound) which was dissolved in water and treated with a little potash and sulphate of copper, due attention being paid to the precautions we have already indicated; after boiling, and especially after long standing, there was a very considerable yellow sediment of suboxide of copper. From the result of this experiment I believe that with from 15 to 20 frogs' livers the presence of sugar in this tissue may be distinctly demonstrated. Moreover, I regard this substance as glucose, and not milk-sugar, in consequence of its reducing the oxide of copper far more slowly than is usually the case with milk-sugar.

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* Buchn. Report. Bd. 42, S. 46.

† Comp. rend. T. 27, p. 514.

Sugar has been sought for in all the fluids in cases of *Diabetes*, and has been so generally found that it is unnecessary to quote authorities on the subject. It has been found not merely in the urine, blood, and all serous fluids, but also in the saliva, in vomited matters, in the solid excrements, and even in the sweat.

In a person suffering from well-developed diabetes, and who at the same time perspired very freely, (a combination not often observed,) it was only in the sweat that I failed to detect sugar.

Origin.—The origin of the small quantities of glucose which normally occur in the animal fluids, is so obvious, as hardly to require notice. I will here only remark that little or nothing in the way of conclusion can be deduced in reference to the metamorphosis of starch or dextrin within the animal organism from experimental attempts to convert starch into sugar by means of saliva, the serum of the blood, renal tissue, &c.; for any other nitrogenous substance acts just as efficiently, if it be digested for a sufficiently long time with water and starch-paste, in converting a portion of the latter into sugar. The actual substance which, in all probability, effects the conversion of starch into sugar, is, as we have already mentioned, the pancreatic juice. Magendie's experiment,* in which starch was converted into sugar in the circulating blood of a living animal, proves little in relation to the physiological process, since starch does not normally pass into the blood. We shall enter more fully in the consideration of the digestion of starch and of the experiments bearing on this point which have been instituted by Bouchardat and Sandras, Jacubowitsch, Strahl, and others, in a future part of the work.

But whence originates the enormous quantity of sugar which, in *diabetes*, is often discharged with the urine? While no one can doubt that it is for the most part, at all events, derived from vegetable food, it is still a contested question whether the nitrogenous constituents of the animal body may not also contribute to the formation of this substance. Many have assumed it as beyond all question (Budge,*) that in diabetes sugar is formed from protein, but, on examining the grounds on which such a view is based, we find that the facts adduced in support of them are of a very doubtful character. In the first place it has been alleged that diabetic patients, living on a highly nitrogenous diet, discharge far more sugar than could be formed from the sugar-yielding, non-nitrogenous substances, which have constituted a portion of their food; but unfortunately no accurate observations on this point, based on numerical results, have been brought forward; for, although Pfeuffer and Löwig† have instituted one experiment of the kind, it led to no result. Moreover, we are still so ignorant regarding the internal constitution of albuminous and gelatinous substances, that we can adduce no chemical grounds in support of such an assumption. Berzelius,‡ founding his hypothesis on the fact that protein, like sugar, when treated with hydrochloric acid, yields formic and humic acids, and, with nitric acid, yields oxalic and saccharic acids (which, however, has not been decisively proved), indicates the possibility that protein (like amygdalin, salicin, &c.) may contain sugar, and that a portion of the diabetic sugar may therefore proceed from the albuminous substances. The supposition is, also, by no means at variance with the admirable investigations of Guckelberger on the products of decomposition of nitrogenous animal tissues by sulphuric acid and chromate of potash; since by this means of oxidation, aldehyde§ is developed from these nitrogenous matters, just as it is produced from milk-sugar when similarly treated. These facts, however, simply indicate the possibility that sugar may be formed from the protein-compounds; they do not prove that it is so formed; Liebig|| merely regards it as "conceivable" that in the metamorphosis of tissue, sugar may be produced from gelatinous substances.

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* Compt. rend. T. 30, pp. 189-192.

Notwithstanding the numerous hypotheses that have been advanced by physicians regarding the reason why, in diabetes, the sugar does not undergo the ordinary change in the organism, we are still utterly ignorant on this point. As we shall return to this subject in the second volume, in our observations on "the urine,"

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* Arch. f. physiol. Heilk. Bd. 3, S. 391.

† Zeitsch. f. rat. Med. Bd. 1, S. 451.

‡ Jahresber. Bd. 19, S. 655.

§ Ann. d. Ch. u. Pharm. Bd. 64, S. 99.

|| Geiger's Pharm. Bd. 1, S. 796.

it will suffice if we here mention the following facts, which may subsequently influence our judgment in reference to this matter.

I* injected two drachms of cane-sugar dissolved in water into the veins of a dog; the dog, who had lost very little blood during the operation, drank a great deal, and discharged a large quantity of sweet-tasting urine, which contained *unchanged* cane-sugar; and Kersting† arrived at a similar result with other kinds of sugar. Bernard‡ injected a solution of cane-sugar into the veins of a dog and a rabbit; the urine of the animals remained acid, and contained unchanged cane-sugar; but, on repeating the experiment on another dog and rabbit with a solution of glucose, he failed to detect this substance in the urine, which had now become alkaline.

[The admirable experiments and observations of Dr. Percy on this subject are apparently unknown to Professor Lehmann. See the "Medical Gazette," Vol. 32, pp. 19, 591, and 640.—G.E.D.]

If we were to attempt to draw any conclusion from these few experiments, it would be that in diabetes the glucose formed from the vegetable substances in the intestine is not, as in the normal state, metamorphosed in the blood. We have been in the habit of referring the alkaline reaction of the urine in graminivorous animals to the decomposition of the salts formed by organic acids and the alkalies into carbonates, but from Bernard's experiment it would appear as if the alkalescence were dependent on other relations connected with the nature of the vegetable food: at all events I found that, when for two entire days I took nothing but sugar, fat, and starch, and consequently food devoid of nitrogen and free from alkalies, my urine had an extremely weak acid reaction.

More accurate investigations, or a more detailed account of his mode of procedure are requisite, before we can form an opinion regarding certain experiments performed by Bernard,§ or can attempt to explain them on physiological grounds. He maintains that he has found sugar in the urine and the blood after irritating one definite spot in the base of the fourth ventricle of the brain. This experiment, if it should receive further confirmation, will apparently strengthen Scharlau's hypothesis that diabetes is essentially a disease of the spinal cord, unless Bernard associates it with the function of the pneumogastric nerves; for when they have been divided he has also found sugar.

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* Jahresber. d. phys. Ch. 1844. S. 47.

† Diss. inaug. med. Lips. 1844.

‡ Compt. rend. T. 22, pp. 534-537.

§ Ibid. T. 28, p. 393, and Arch. gén. de Méd. 4 Sér. T. 18.

Uses.—Since glucose, which, as we have already seen, is principally formed in the intestinal canal from the starch of the vegetable food, appears, from the results of all physiological enquiries, to be a true element of nutrition, (see "Nutrition,") the question that remains to be considered is—how it is applied, or what is its use in the animal organism? It belongs, according to Liebig, to the food for the respiration; and if we regard it purely in this light, its object is easily understood; it undergoes a process of combustion by combining with the inspired oxygen, its final products being water and carbonic acid, and tends to support the animal heat, if we regard this as an independent process. If, however, we entirely concur in this view, we have still to enquire whether the sugar does not previously undergo other changes and serve other objects, before it yields carbonic acid and water as the final products of its combustion.

It must excite our surprise that in diabetes, where, in reference to the respiration, the saccharine and amylaceous elements of food appear to be entirely lost, the respiration and the animal heat are so well supported; for although pulmonary tuberculosis is a frequent complication of diabetes, this is by no means invariably the case; and it may occur without any affection of the lungs. It certainly seems very remarkable that such a mass of the respiratory food can be lost without inducing any symptom of a disturbed respiration or of a diminished animal heat.

We have already referred (p. 257) to the hypothesis of the conversion of sugar in the intestinal canal into *fat*, and shown that it is unsupported by facts; but we do not deny that in some part of the animal body (at least under certain relations) sugar may be metamorphosed into fat. Moreover, we are still so ignorant regarding the different changes which the sugar undergoes in the blood, that, to a certain degree, we must content ourselves with the consideration of questions that may lead us on the true path of inquiry. We have already pointed out the probability that the *lactic acid* occurring in the animal body is formed from sugar (p. 101); under special relations *butyric acid* may also be produced from it (p. 59). The alkalescence of the urine observed by Bernard after the injection of glucose would almost seem to indicate that the sugar in the blood is converted into an acid, which, combining with the alkali of the blood, yields carbonated alkali as a product of combustion, which passes into the urine and renders it alkaline. This experiment undoubtedly shows that the principal metamorphosis of the sugar occurs primarily in the blood, and not in the intestinal canal.

That the sugar undergoes *vinous fermentation* in the intestinal canal is a view that is now entirely rejected; for the yeast-corpuscles which we sometimes find in the contents of the intestines, and which might lead to the suspicion of such a fermentation, may take their origin from the food, as, for instance, from bread.

Does the sugar take any part in the formation of bile? We have already attempted (see p. 126 and p. 270) to show the probability that the bile is in part formed from fat, and that cholic acid should be regarded as conjugated oleic acid with the adjunct $C_{12}H_6O_6$. Can this adjunct take its origin from the sugar?

Those who assume that sugar exists preformed in nitrogenous animal substances, whether gelatinous or albuminous, (as for instance it does in amygdalin,) need feel no difficulty in believing that in the animal body protein is primarily formed from nitrogenous matters and sugar. In the case of chitin, however, (to which further reference will be made in a future page,) we appear rather to have a combination of vegetable fibre with a nitrogenous substance.

We can hardly entertain a doubt that in the female mammalia the milk-sugar is derived from the glucose, but by what means this change is accomplished is a point on which we are entirely ignorant.

MILK-SUGAR.—$C_{10}H_8O_8$.

Chemical Relations.

Properties.—This substance forms white, opaque, overlying prisms or rhombohedra containing 2 atoms of water, is hard, craunches between the teeth, has a very faintly sweet, almost floury taste, is devoid of smell, dissolves slowly in cold but more readily in hot water, and is insoluble in absolute alcohol and ether; the aqueous solution which moreover turns the plane of polarisation of a ray of light to the right, may be evaporated to a very considerable extent without any separation of the sugar in a crystalline form.

When heated, milk-sugar melts, swells up, developes a sweetish pungent odour, and burns with a flame.

Digested with dilute sulphuric or hydrochloric acid, or with acetic or citric acid, it becomes converted into glucose; it absorbs large quantities of chlorine, hydrochloric acid, and ammoniacal gases. Nitric acid converts it into mucic acid with a little oxalic, saccharic, and carbonic acid; with sulphuric acid and bichromate of potash it yields not only formic acid but aldehyde.

In contact with the caustic fixed alkalies it becomes converted at 225° into oxalic acid; boiled with dilute alkalies or oxide of lead and water it becomes yellow or brown; at 50° it yields several compounds with oxide of lead. It reacts with sulphate of copper and potash exactly in the same manner as glucose. It was for a long time classed among the non-fermentable kinds of sugar, till Schill* and Hess† almost simultaneously remarked that milk-sugar only required a longer period in order to pass into a state of vinous fermentation under the influence of yeast, sour dough, gelatin, or albumen. H. Rose‡ has confirmed Schill's observations, that the formation of dextrin must precede the vinous fermentation of the milk-sugar, as indeed Payen had previously observed in reference to the sugar of the dahlia, and Rose in reference to cane-sugar. Like the other varieties of sugar, it can undergo lactic and butyric fermentation when the necessary ferments are added to it.

Composition.—In its crystalline state milk-sugar has exactly the same empirical formula as anhydrous glucose, so that it therefore contains equal equivalents of carbon, hydrogen, and oxygen. But as, when warmed, it loses 11·9% of water, that is to say, 1 atom of water to 5 atoms of carbon, its formula must either $= C_5H_4O_4$ or a multiple of it. As milk-sugar cannot be combined with any body in a definite proportion, its true atomic weight is unknown. Its relation to nitric acid, with which, as we have already mentioned, it yields mucic acid, shows that its constitution must in some respects be different from that of the other fermentable sugars.

Preparation.—Milk-sugar is obtained on the large scale by evaporating whey, and allowing the concentrated fluid to stand for a long time in a cool place. The crystalline incrustations which are then formed are purified by recrystallisation. Simon recommends that the milk should be evaporated to ⅛th of its volume, and that the casein should be precipitated by alcohol; the filtered fluid must be then further evaporated and treated with strong alcohol; the milk-sugar, which is precipitated with the water-extract, is then rinsed with a little water, dissolved in pure water, and left to spontaneous evaporation.

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* Ann. d. Ch. u. Pharm. Bd. 31, S. 152.

† Pogg. Ann. Bd. 31, S. 194.

‡ Ibid. Bd. 52, S. 293.

According to Haidlen* the milk should be boiled with ⅕th its weight of pulverised gypsum, which coagulates the casein; the filtered fluid is then to be evaporated to dryness, and after the fat has been removed by ether, the milk-sugar may be extracted from the residue by boiling alcohol, which yields it in a state of perfect purity.

Tests.—If it be shown by Trommer's test that some kind of sugar is contained in the alcoholic extract of an animal fluid, we may readily distinguish milk-sugar from other kinds of sugar (if we have a sufficient amount of material to examine,) by its difficult solubility in alcohol, by the slowness with which it ferments in the presence of yeast, and by its property of yielding the insoluble mucic acid when boiled with nitric acid. It may be estimated *quantitatively* with tolerable accuracy by Haidlen's method given above; but when extreme accuracy is required we must use Barreswil's or Fehling's test-fluid, in the manner described for grape-sugar (see p. 287); Poggiale has in this way determined the sugar in cow's milk by a test-fluid (consisting of 10 parts of crystallised sulphate of copper, 10 of bitartrate of potash, 30 of caustic potash, and 200 of distilled water), but his results were obviously in excess; for although he attempted to remove the casein previously with acetic acid, a portion of this substance must have remained in solution and coöperated with the sugar in decomposing the oxide of copper. A better method of proceeding is to remove the casein by boiling the milk with sulphate of magnesia or chloride of calcium, precipitating any excess of the earth from the filtered fluid with potash, and then applying Fehling's test-fluid; while perhaps the best is to proceed according to Haidlen's plan, and then to apply Fehling's method to determine the quantity of milk-sugar in the alcoholic extract.

Physiological Relations.

Occurrence.—This substance appears to be an integral constituent of the milk of all mammalia. In woman's milk its amount ranges from 3·2 to 6·24% (Fr. Simon,† Haidlen,‡ Clemm,§); in cows' milk it is stated to average from 3·4 to 4·3%; but by an improved method of analysis I have always found rather a larger amount of sugar in good cows' milk; but the average (=5·28%)

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* Ann. d. Ch. u. Pharm. Bd. 45, S. 275.

† Frauenmilch. S. 35.

‡ Ann. d. Ch. u. Pharm. Bd. 45, S. 275.

§ Handwörterbuch d. Phys. Bd. 2, S. 464.

assumed by Poggiale[*] is obviously too high; in that of the ass it constitutes 4·5%; in that of the mare, 8·7%, in that of the goat, 4.4% and in that of the sheep, 4·2%; indeed, it was even found in the milk of a he-goat. (Schlossberger.[†]) Dumas[‡] thought that he had ascertained that the milk of bitches restricted entirely to an animal diet contained no milk-sugar, but it was subsequently ascertained by Bensch[§] that even then traces of milk-sugar were present; its quantity is however perceptibly increased under the use of a vegetable diet.

In the colostrum Simon found 7%, and in the milk six days after delivery only 6·24% of milk-sugar; his investigations show that it diminishes according to the length of time after delivery at which it is secreted, and that neither an *abundant* nor an *insufficient diet* influences its quantity, although differences in the food considerably affect the amount of butter. The observations of Donne,[‖] Meggenhofen,[¶] and Simon[**] concur in showing that *diseases*, especially syphilis, do not modify the amount of sugar in the milk.

Milk-sugar has been sought for in the *blood* by Mitscherlich, and Tiedemann and Gmelin, but hitherto without success.

[Braconnot[††] believes that he has demonstrated that milk-sugar exists in the cotyledons of the seeds of vegetables.—G. E. D.]

Origin.—The positive experiments of Dumas and Bensch which prove that the amount of milk-sugar increases during a vegetable diet, give great probability to the opinion that this substance is principally formed from glucose or from the starch of the food; but notwithstanding the apparently affirmative observations of Bensch, the question whether it may not also be formed from nitrogenous matters, must for the present remain undecided. Where and by what means this conversion of glucose within the organism occurs, are subjects of which we are entirely ignorant.

Uses.—No doubt can be entertained that the milk-sugar which the infant at the breast receives in its food serves the same purposes in the economy that starch and other carbo-hydrates serve in the more matured organism.

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[*] Compt. rend. T. 28, pp. 505-7.

[†] Ann. d Ch. u. Pharm. Bd. 51, S. 431.

[‡] Compt. rend. T. 21, pp. 708-717.

[§] Ann. d. Ch. u. Pharm. Bd. 61, S. 221-227.

[‖] Du lait et en particulier de celui des nourrices. Paris, 1836.

[¶] Diss. inaug. sist. indagationem lactis muliebris. Francof. a. M., 1816.

[**] Die Frauenmilch. Berlin, 1838.

[††] Ann. de Chim. et de Phys. 4 Ser. T. 27, p. 399.

A carbo-hydrate has been found in some of the lower classes of animals whose composition and properties are very similar to those of the vegetable principle, *cellulose*. C. Schmidt* discovered it in the mantel of ***Phallusia mammillaris***, one of the mollusca belonging to the Tunicata; and Löwig and Kölliker† have subsequently recognised it in the cartilaginous capsule of the simple Ascidiæ, in the leathery mantle of the Cynthiæ, and in the outer tube of the Salpæ. The relation which this substance bears to chitin as well as to the animal organism generally, will be noticed in our remarks on chitin.

COLOURING MATTERS.

Unfortunately, even less is known of the chemical nature of the animal than of the vegetable pigments, so that we must still retain the irrational system of arranging them according to colour.

HÆMATIN.—$C_{44}H_{22}N_3O_6Fe$.

Chemical Relations.

Properties.—This substance is regarded as the peculiar red pigment of the blood-corpuscles; but unfortunately it is by no means certain whether it is a product of metamorphosis of the true colouring matter of the blood, or whether the substance prepared by us only bears the same sort of relation to that which exists in the blood-corpuscles as coagulated albumen bears to that principle in its fluid state. We cannot isolate it in its soluble state from the globulin of the blood-corpuscles; hence we are only acquainted with it in its coagulated (and essentially modified) condition. In a state of purity it occurs as a dark brown, slightly lustrous mass, which, on trituration, adheres to the pestle; it is devoid of taste and smell, and is insoluble in water, alcohol, ether, acetate of oxide of ethyl, and fatty and volatile oils: Mulder, however, regards it as slightly soluble in fatty and ethereal oils.

Hæmatin dissolves very readily in weak *alcohol* to which sulphuric or hydrochloric acid has been added, forming a brown solution, which, on saturation with an alkali, assumes a blood-red colour. *Water*, acidulated with the same acids, exerts no solvent power on hæmatin, and consequently a precipitation is induced by the addition of water to alcoholic solutions of this substance. Concentrated sulphuric and hydrochloric acids do not dissolve hæmatin, but they abstract a little of the iron. After trituration with sulphate of soda, it dissolves for the most part in water. Even very dilute solutions of the caustic *alkalies* or their carbonates in water or alcohol dissolve hæmatin in almost every proportion. A potash-solution, boiled and then saturated with an acid, yields a form of hæmatin which is no longer soluble in a mixture of alcohol and ammonia. The potash-solution, on boiling, assumes first a dark red, and subsequently a green tint. The ammoniacal solution gives off its ammonia during evaporation; moreover, hæmatin does not absorb ammoniacal gas. The colour of the ammonia-solution of hæmatin is not affected by *carbonic acid, oxygen*, or *nitric oxide;* sulphurous acid gives it a bright red tint, and sulphuretted hydrogen makes it slightly darker.

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* Zu vergl. Physiol. der wirbellosen Thiere. 1845. S. 62 [or Taylor's Scientific Memoirs, vol. 5, p. 34.—G. E. D.]

† Ann. de Scienc. Nat. 3 Sér. T. 5, pp. 193-232.

Hæmatin is completely precipitated from its ammonia-solution by the *salts of oxide of silver, of lead, and of copper;* if the solution of hæmatin in alcohol, acidulated with sulphuric acid, be boiled with oxide of lead, it becomes entirely decolorised.

When *heated* in an enclosed space, hæmatin puffs up, and, without melting, yields empyreumatic ammoniacal vapours and a reddish brown oil, and leaves a rather small porous charcoal, which on combustion yields a red ash. *Phosphorus* and *sulphate of protoxide of iron* may be boiled with hæmatin without in any way affecting it.

Treated with concentrated *nitric acid* in the cold, it dissolves into a brown fluid, and developes nitrous acid; when boiled with this acid it is entirely destroyed.

If *chlorine* be allowed to act on hæmatin mixed with water, all the iron of the hæmatin dissolves as perchloride of iron, and there is a deposition of white flocculi, which are soluble in alcohol and ether but not in water, develope a little chlorous acid when dried (at 100°), and then form a light straw-coloured powder. This powder is unaffected by hydrochloric acid, but dissolves in alkalies, forming a reddish solution; according to Mulder, it consists of chlorous acid and hæmatin freed from its iron. If chlorine gas be passed over dry hæmatin, they unite and form a dark green compound which is soluble in alcohol, exerts no action on vegetable colours, is unaffected by acids and alkalies, but which, when warmed with hydrosulphate of ammonia, assumes a red colour.

On passing dry *hydrochloric acid gas* over dry hæmatin, there is formed a violet mass, which is soluble both in water and alcohol, communicating to those fluids a red colour and an acid reaction.

If hæmatin be allowed to remain for some time in contact with pure concentrated sulphuric acid, and the fluid be then diluted with water, there is a development of hydrogen gas, and sulphate of protoxide of iron is taken up in solution. By a repetition of this process the whole of the iron, with the exception of a mere trace, may be removed from the hæmatin, without depriving it of its properties and without altering its elementary composition, as far as the relative amounts of the carbon, hydrogen, nitrogen, and oxygen are concerned.

We are indebted to Mulder and van Goudoever[*] for the preparation of hæmatin free from or poor in iron; Sanson and Scherer[†] had, however, previously observed that concentrated sulphuric acid could extract all the iron from the clot or the residue of the blood-corpuscles, without affecting its dark brown colour.

Composition.—Mulder[‡] has calculated, from his analyses, the formula we have given for hæmatin, according to which it contains:

Carbon	.... 44 atoms	65·347
Hydrogen	.... 22 „	5·445
Nitrogen	.... 3 „	10·396
Oxygen	.... 6 „	11·881
Iron	.... 1 „	6·931
		100·000

Mulder's analyses of hæmatin free from iron coincide with the formula $C_{44}H_{22}N_3O_6$. From the chloride of hæmatin Mulder calculates that the atomic weight of hæmatin is 5175.

Chloride of hæmatin, formed from dry chlorine gas and hæmatin, consists of 1 equivalent of hæmatin, and 6 equivalents of chlorine; how this combination may be supposed to be formed, is a point on which at present we can offer no conjecture. The compound obtained from dry hydrochloric acid gas and hæmatin consists, according to Mulder, of 2 equivalents of hæmatin and 3 equivalents of hydrochloric acid; on exposing this substance to a heat of 100°, it loses half its acid, and then consists of 4 atoms of hæmatin and 3 atoms of acid. In the combinations of hæmatin with metals it appears from an experiment of Mulder's that 1 atom of hæmatin is combined with 1 atom of base.

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[*] Journ. f. pr. Ch. Bd. 325, S. 186, ff.

[†] Ann d. Ch. u. Pharm. Bd. 40, S. 30.

[‡] Journ. f. pr. Ch. Bd. 28, S. 340.

The question—in what condition does the iron exist in the blood, or on what iron-compound is its red colour dependent? is one that has long engaged the attention of chemists and physiologists. Without considering that, with an equal right, we might inquire into the causes of the colour of indigo, carmine, or peroxide of iron, it was universally believed that the blood's colour must depend on the last named substance, and consequently, all experiments on the subject were instituted with the view of ascertaining in what state of combination the peroxide of iron lay concealed. It would be superfluous for us to notice the different views regarding the combinations in which the peroxide of iron has been supposed to exist in the blood. We must not, however, omit all notice of the circumstance, that a discovery of Engelhardt's showed the fallacy of these views, for he ascertained that the iron of the blood might be precipitated by alkalies and liver of sulphur, if chlorine gas had been previously, and for some time, passed through the blood; and this led him to the somewhat illogical conclusion that the iron could not be oxidised, but must exist in a metallic state in the blood; for Rose's discovery that the precipitation of peroxide of iron and other metallic oxides may be prevented by all the non-volatile organic acids, shows that notwithstanding Engelhardt's experiment, the iron may be contained in the blood in the state of peroxide. Finally, Lecanu discovered the true colouring matter of the blood, the hæmatin; and as almost all the iron of the blood is contained in this substance, attempts were again made to refer the colour of this pigment to peroxide of iron. But we know, from the experiments of Scherer, Sanson, and Mulder, that the iron must be contained in some other combination than in direct combination with oxygen, and that the iron may be abstracted from the red blood-pigment without affecting its colour. That the iron is directly combined with the group of atoms constituting hæmatin, is not a probable view; at present, however, we are in possession of no facts throwing any additional light on the nature of the iron-compound.

The white body formed by the action of chlorine and water on hæmatin, was found by Mulder to be devoid of iron, and to be composed in accordance with the formula $C_{44}H_{22}N_3O_6+6ClO_3$.

Preparation.—We treat blood with about eight times its volume of a solution of sulphate of soda or chloride of sodium, filter it, and wash the residue on the filter as thoroughly as possible with the same saline solution; the residue thus almost completely freed from serum, or, in other words, the mass of the blood-corpuscles, is dissolved in water, and coagulated by the application of heat; the washed, dried, and finely triturated coagulum is now boiled with spirit containing sulphuric acid, till the fluid passes through a filter in a decolorised state. This filtered fluid, which in the mass presents a brownish-red tint, after being saturated with ammonia, deposits sulphate of ammonia and a little globulin; these being removed by filtration, the fluid is evaporated to dryness; the solid residue is extracted with water, alcohol, and ether, and in order to effect the complete removal of any adhering globulin, is again dissolved in spirit containing ammonia; the solution is then filtered, evaporated, and the residue extracted with water.

Tests.—If from any suspicion of the presence of blood we wish to examine a fluid for hæmatin, it is by far the best plan to employ the microscope, and by its means to endeavour to detect blood-corpuscles, or their fragments. It only rarely happens, in certain exudations or saturated masses in which blood-corpuscles are no longer present, that we can with certainty recognise the red pigment of the blood, since its quantity is so small, that we can scarcely obtain enough, by the methods we have given, to apply any tests to it.

That the *hæmatoidin* discovered, or at least first accurately investigated by Virchow,* (the same substance which has also been named *xanthose*) is not perfectly identical with hæmatin is obvious from Virchow's experiments; but the occurrence of this substance in sanguineous extravasations, whose metamorphoses have been most admirably traced out by Zwicky, Bruch, and Virchow, denotes as decidedly as chemical experiments could do, that it is formed from hæmatin; moreover, several of its properties indicate its close affinity with the last named substance.

Hæmatoidin occurs in an amorphous condition in granules, globules, and jagged masses, as well as in perfectly formed crystals of the monoclinometric system; these latter are oblique rhombic prisms, not unlike crystals of gypsum, but frequently are almost perfect rhombohedra; they are strongly refractive and transparent, are of a yellowish-red, red, or ruby colour, and are insoluble in water, alcohol, ether, acetic acid, dilute mineral acids, and alkalies. I have sometimes seen the smaller and less deeply coloured crystals dissolve in alcohol containing sulphuric acid or ammonia, and be again precipitated by neutralisation of the fluid; this is, however, not invariably the case. Virchow has very carefully examined the behaviour of this body with concentrated alkalies and mineral acids; these agents, however, do not act in precisely the same manner on all specimens of this pigment; on the addition of hydrate of potash, a fiery red tint is developed, the mass becomes gradually loosened in its texture, and becomes disintegrated into red granules which at length dissolve; on neutralising the alkali the substance is, however, not again precipitated. When a concentrated mineral acid, sulphuric acid, for example, acts on it, it causes the sharp outlines of the crystals to disappear; and the colour of the roundish fragments, after first becoming brownish-red, passes through successive shades of green, blue, and rose-tint, till it finally terminates in a dirty yellow. Iron may sometimes, but not always, be detected in the acid fluid containing the decomposed hæmatoidin.

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* Arch. f. pathol. Anat. u. s. w. Bd. 1, S. 383-445.

Hæmatoidin may always be found in the sanguineous extravasations occurring in consequence of the bursting of the Graafian vesicles at the periods of menstruation or conception, and frequently occurs in old extravasations in the brain, in obliterated veins, hæmorrhagic infarctus of the spleen, in subcutaneous sugillations, and in purulent abscess of the extremities. (Virchow.) It appears from Virchow's observations that these crystals may form from seventeen to twenty days after the occurrence of the extravasation. Kölliker* has observed the formation of crystals of this nature within the corpuscles in the blood of certain fishes; these crystals were however, soluble in acetic acid, potash, and nitric acid.

Although every care and precaution have been taken, both Virchow and I have failed in obtaining these crystals of modified hæmatin either from solutions of blood or of hæmatin itself; but yet those who still assign an important part in the animal body to vital forces, must grant that under the necessary conditions, hæmatoidin may be produced out of the body from hæmatin, since this kind of metamorphosis occurring in extravasations in all respects exhibits the character of a disintegration, that is to say, of a purely physical and chemical process. Moreover, Kölliker's observation gives us room to hope that we may be able to obtain crystallisable hæmatin or hæmatoidin from the blood of the lower animals,—fishes, for example,—so as to submit it to an accurate chemical examination.

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* Zeitschr. f. wiss. Zoologie. Bd. 1, S. 266.

Physiological Relations.

Occurrence.—Hæmatin has hitherto only been found in the blood-corpuscles of the higher animals. Intimately united with globulin, it forms the viscid, fluid contents of the coloured blood-cells.

Berzelius found 0·38% of metallic iron in the dried blood-corpuscles of man or the ox; now as Mulder has found 6·64% of iron in hæmatin, a simple calculation shows that in the blood-corpuscles there are contained 5·72% of hæmatin, independently of fat, globulin, salts, and biliary matter: hence, in fresh blood in which the red blood-corpuscles on an average =12·8%, there would be contained 0·732% of hæmatin. If we calculate from Becquerel's results, according to which 1000 parts of blood contain 0·565 parts of iron and 141·1 of blood-corpuscles, we obtain a very similar result, namely, that 100 parts of blood-corpuscles contain 6·02 of hæmatin. It is obvious that such calculations can only lead to approximate results; attempts have certainly been made to effect a direct determination of the amount of hæmatin in the blood; but the method of separating it is as yet too uncertain to admit of our placing much reliance on the numbers which have been obtained. The amount found in the blood by Lecanu, namely 0·227%, was obviously too small, while Simon's number, 0·718%, approximates closely to the calculated quantity.

By treating defibrinated calves' blood with chloride of sodium, Schmidt obtained the corpuscles in a state of purity; and after incineration, found in them 1·179% of peroxide of iron, hence, (according to Mulder's analysis of hæmatin,) they would contain 12·41% of this ingredient; in repeating Schmidt's experiment with ox-blood I obtained 9·076 and 10·94% of peroxide of iron—results which corresponded tolerably well with that which he found. The great difference which presents itself between these results of direct experiment, and the results of pre-indicated calculations, admits of an easy explanation; in the latter case, the blood-corpuscles are calculated more or less in accordance with their true constitution in the blood, while in our experiments, the process by which we purify the blood-corpuscles—their treatment with a solution of chloride of sodium or sulphate of soda—abstracts from them a portion of their globulin, and all the soluble salts; when treated with saline solutions, the corpuscles lose, in accordance with the laws of endosmosis, not only water, but also a part of their soluble globulin; while the treatment of the coagulated corpuscles wi water, alcohol, and ether, abstracts from them all soluble salts, and the fat, which in itself amounts, according to my investigations, to at least 2%.

The ratio of the hæmatin to the blood varies in *diseases* for the most part with the number of the blood-corpuscles; but whether the ratio of the hæmatin to the globulin of the blood-corpuscles be constant, or whether the hæmatin be liable to greater variations than the globulin, are questions which in the present state of organic analysis it is impossible to answer.

Origin.—There is nothing in the chemical constitution of hæmatin which throws any light on the mode of its formation; we do not know whether it is directly formed from the constituents of the food or from the products of metamorphosis of effete tissue; and we have no certain knowledge regarding the part of the organism in which it is produced. The chyle certainly contains iron, and hæmatin exists in the thoracic duct; but iron is not hæmatin, and the small quantity of the last-named substance may have passed from the blood through the mesenteric glands into the chyle, or may have arisen from the blood-corpuscles which have passed with the splenic lymph into the chyle. If the formation of hæmatin took place in the chyle it would not be after prolonged fasting that we should find it richest in this substance. Chemistry, as we have already observed, affords us no assistance in reference to the formation of this body; we must, therefore, at present, confine our attention to physiological facts, in order that we may obtain a safe starting-point for further chemical enquiries.

Most physiologists of the present day coincide in the opinion that the red blood-corpuscles are developed from the colourless ones; but whether they regard the former as nuclei of the latter, or as independent cells produced from them—whether they adopt the views of H. Müller,[*] of Gerlach,[†] or of Kölliker[‡]—they must in any case admit that the red pigment of the blood is primarily formed within the enveloping membrane of the cell. Further, physiological enquiry demonstrates, almost beyond a doubt, that the blood pigment is first formed in the perfected cells, and, moreover, affords us some indication, however indistinct, of the source from whence this pigment may possibly have been produced. Nasse, Hünefeld, and others, have proved that the granular matter visible in many of the coloured blood-corpuscles is merely fat; indeed in the yolk-cells, in the young blood-corpuscles of the amphibia [in their embryonic state] we find not only roundish but also angular granules soluble in ether, which can hardly be anything else than stearin. Henle and H. Müller refer the primary origin of the colourless blood-corpuscles to the fat which is recognisable as a fine granular (almost cloudy) matter in the minutest lacteals. We have already mentioned that the fat stands in a certain relation to the functions of the liver; the beautiful investigations of E. H. Weber and Kölliker have, however, now demonstrated that large quantities of blood-corpuscles are always formed in the liver in the fœtal state, and during the hybernation of certain animals, and therefore at periods when this organ secretes little or no bile, but when fat is accumulated in it.

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[*] Zeitschr. f. rat. Med. Bd. 3, S. 204-278.

[†] Ibid. Bd. 7, S. 70-90.

[‡] Ibid. Bd. 4, S. 112-160.

Moreover, an unprejudiced examination of the development of the chick within the egg leads to the assumption that the fat takes a part in the formation of hæmatin; and if physiological facts can be adduced in favour of this hypothesis, there are at all events no chemical objections to it. As it is obvious that the colouring matter can only be formed when there is free access of oxygen, namely in the vessels, and as the oxygen doubtless contributes materially to its production, we cannot suppose that it is formed from protein, which is a substance rich in oxygen, or from sugar; hence there is hardly any other substance than the fat from which a process of oxidation could yield hæmatin.

Our present assumption of the formation of hæmatin from fat is to be regarded merely as an hypothesis based on one or two physiological facts, which may possibly admit of a very different interpretation; it is only intended to serve as a means of directing our attention in a definite direction in the investigation of this subject.

Uses.—The constant occurrence of hæmatin in the blood-corpuscles indicates that this body takes an important part in the metamorphosis of the animal tissues. All sorts of conjectures have been hazarded regarding its function in the blood, and it has been especially supposed to be connected with the process of respiration. In point of fact, however, it is unnecessary to consider any hypothesis, until it has been satisfactorily ascertained whether the hæmatin in question actually stands in the same relation to the true pigment of the blood as coagulated to non-coagulated albumen, or whether artificially prepared hæmatin is altogether a product of decomposition of the actual pigment. If hæmatin has the same composition as that which we prepare artificially, and if the only difference be that it exists in a soluble form in the blood-corpuscles, there is at once an end to all those very imaginative hypotheses which assume that the iron takes a great share in the process of respiration, and that it is the conveyer of oxygen to the blood.

The experiments of Bruch[*] on the action of gases on the colour of the blood, and the observations of Harless,[†] regarding the gradual destruction of the corpuscles of frogs' blood, certainly indicate that there is a chemical action between the blood-corpuscles and their contents on the one hand, and the inspired oxygen on the other, in which action the hæmatin doubtless participates.

The observations of Hannover,[‡] which show that persons whose blood is very deficient in red corpuscles (chlorotic persons) exhale as much carbonic acid as healthy persons, seem on the other hand to contra-indicate a direct relation between the blood-corpuscles or blood-pigment, and oxidation in the blood. We must, therefore, give up for the present all attempts at understanding the function of the blood-pigment.

The question as to what becomes of the hæmatin when the blood-corpuscles and their contents undergo disintegration, is one which for a long time was enshrouded in perfect obscurity, but on which some light has now been thrown by Virchow's admirable investigations on hæmatoidin. The occurrence, in a crystalline form, of this substance, which is undoubtedly derived from the blood-pigment, and its different behaviour towards the same reagents, indicate that, notwithstanding its crystalline arrangement, it continues to undergo changes which give rise to a substance perfectly similar to, if not identical with, bile-pigment or melanin. Although the subject is still far from being satisfactorily settled, Virchow was the first who by his pathologico-histological and chemical investigations prominently brought forward definite facts which have afforded the first solid groundwork for the hypothesis which was long since propounded, that hæmatin might be transformed into cholepyrrhin.

In reference to this point we would specially direct attention to Virchow's ingenious treatise, in which he endeavours to strengthen the view regarding this metamorphosis by means of a simple induction based on direct observation. It has unfortunately hitherto been found impossible to separate hæmatoidin in so pure a state and in sufficient quantities as to admit of its being subjected to a rigid chemical investigation. From Virchow's investigations it is, however, apparent that the physician must also lend his help for the advancement of pathological and physiological chemistry; for without the aid of pathological histology,—without a judicious application of the microscope,—the chemist could not have succeeded in discovering hæmatoidin any more than in detecting oxalate of lime in normal urine; without such aid the chemist could never have conceived an idea of the metamorphosis of the pigments in the animal body. As long as the physician contents himself with borrowing mere hypotheses from chemists, without being himself practically familiar with chemical science, he can never hope to gain the advantages which it is capable of affording; in this respect he resembles the agriculturist, who can never expect to raise his pursuit to the dignity of a science until he has learned the practical application of the principles of chemistry.

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[*] Zeitschr. f. rat. Med. Bd. 3, S. 308.

[†] Ueber den Einfluss der Gase auf die Blutkörperchen von Rana tempor. Erlangen, 1846.

[‡] De quantitate acidi carbonici ab homine sano et aegroto exhalati. Hauniæ, 1845.

MELANIN.

Chemical Relations.

Properties.—Melanin forms either a black, cohesive mass, or a blackish-brown powder; it is devoid of smell and taste; when stirred in water it continues to float for some time, but is insoluble both in water and in alcohol, in ether, in dilute mineral acids, and in concentrated acetic acid; it dissolves, after prolonged digestion, in a dilute solution of potash, from which it is again precipitated with a light brown colour by hydrochloric acid; it is decomposed when boiled with concentrated nitric acid, but it is not affected even by the very prolonged action of chlorine. It is a conductor of electricity, is incapable of fusing, may be ignited in the air, and burns with a vivid light, the charcoal continuing to smoulder till it is reduced to a whitish-yellow ash consisting of chloride of sodium, lime, bone-earth, and a little peroxide of iron. By dry distillation it yields an empyreumatic substance, and carbonate of ammonia. According to Gmelin this pigment is rendered paler, and is partially dissolved by chlorine-water, the undissolved portion becoming again of a dark brown colour on the addition of potash.

Whether the black crystals which have been found by Mackenzie,[*] Guillot,[†] and Virchow,[‡] in melanotic masses are or are not identical with melanin, is a question which, with our present very imperfect knowledge of this pigment, must still remain undecided. Virchow found these crystals to be flat rhombic tablets with extremely acute angles.

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[*] A Practical Treatise on Diseases of the Eye. Lond. 1835. p. 663.

[†] Arch. gén. de Méd. 4 Sér. T. 7, p. 166.

[‡] Arch. f. pathol. Anat. u. s. w. Bd. 1, S. 399.

Composition.—Scherer* gives the following as the mean result of three analyses of this body:

Carbon	58·084
Hydrogen	5·917
Nitrogen	13·768
Oxygen	22·231
	100·000

As we are neither acquainted with the atomic weight of this body, nor with any of the products of its decomposition, we cannot attempt to construct a hypothetical formula for it. In the pigment from the choroid coat of the eye I found 0·254% of iron.

The black pigment which is often deposited as a morbid product in the lungs presents great differences of composition. In two different cases which C. Schmidt† analysed he found:

Carbon	72·95	66·77
Hydrogen	4·75	7·33
Nitrogen	3·89	8·29
Oxygen	18·41	17·61
	100·00	100·00

Preparation.—The best method of obtaining this body is from the eye, by removing the retina, and detaching the choroid coat from the sclerotic. The choroid coat must be placed in a clean rag, and the colouring matter washed out with pure water, just as the starch-granules in the preparation of gluten are washed out through linen bags; the pigment remains for a long time suspended in the water, from which, however, it may be readily removed by filtration, or the fluid may be evaporated and the residue extracted with water.

Tests.—The physical properties of this body are so characteristic, that it is easy to recognise and to separate it; generally, however, it only occurs in such small quantities that it is impossible to distinguish whether the object in question is identical with the melanin of the eye, especially as we still know comparatively little regarding the chemical characters of this last-named substance. No conclusions regarding the presence of black pigment can be drawn from mere colour and insolubility in different menstrua, since as Jul. Vogel[*] was the first to observe, the tissues may be infiltrated with sulphide of iron, from which, however, the black pigment may very readily be distinguished by means of acids.

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* Ann. de Ch. u. Pharm. Bd. 40, S. 6.

† *Vogel's pathol.* Anat. S. 161 [or English Translation, p. 192.]

Physiological Relations.

Occurrence.—This pigment exists as a thick investment on the choroid coat of the eye. Whether it also occurs in other parts of of the animal organism, is a point which cannot be decided, since the other pigments of the same colour in morbid depositions either have not been accurately analysed, or from their very small quantity do not admit of analysis; as for instance, the pigment of the black bronchial glands, of the *rete mucosum seu malpighianum* of the negro, of melanotic tumours, of the black serum which has been occasionally observed, and of pulmonary tissue in certain cases.

In the choroid coat the melanin is enclosed in peculiar hexagonal cells, but in the coats of the blood-vessels of frogs and other amphibia it is found in jagged ramifying cells. In other parts of the animal body—in melanotic tumours for instance—it occurs, however, merely scattered among other cells or tissues. Whether granular cells, when becoming obsolete, (such for example as we find in old exudations,) contain actual melanin, is a question which must still remain undecided. Sanguineous extravasations are, however, not unfrequently converted into a mass, which is coloured perfectly black by black pigment.

Origin.—The large quantity of iron contained in this pigment indicates that it takes its origin from the hæmatin. We cannot recognise such a conversion by chemical means, till we are able to demonstrate that pathological depositions of pigment contain true melanin. Whatever view we may adopt regarding the production of the black-coloured inflammatory globules, we must at all events agree with Bruch[†] that they contain blood-pigment and the rudiments of blood-corpuscles, even if we do not, like Hasse[‡], H. Müller, and Pestalozzi[§], see true blood-corpuscles in these cells; if we examine the expectoration in a case of pneumonia in which resolution is very gradually progressing, we find, on making a perfectly unprejudiced observation, very many of these cells which have the exact colour of blood-corpuscles. Virchow[||] has very accurately traced, by microscopical examination, the conversion of isolated coagula in obliterated veins into amorphous and crystalline pigment, and from these morphological investigations it can hardly be doubted, that at all events the melanin of morbid products is formed from the hæmatin. Kölliker[*] has moreover convinced himself that in the blood-corpuscles enclosed in the enveloping membrane, the hæmatin affords the matter from which the black pigment in the granular cells is formed. Hence it only remains for the chemist to continue his investigations on this subject, in order to obtain perfectly satisfactory scientific proof of this metamorphosis.

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[*] Pathol. Anat. S. 163 u. 311 [or English Translation, pp. 194 & 396.]

[†] Untersuch. zur Kenntniss des körnigen Pigments der Wirbelthiere. Zurich, 1844. S. 42 ff, and Zeitschr. f. rat. Med. Bd. 4, S. 24 ff.

[‡] Zeitschr. f. rat. Med. Bd. 4, S. 1-15.

[§] Ueber Aneurismata spuria der kleinen Hirnarterien u. s. w. Würzb. 1849.

[||] Arch. f. pathol. Anat. u. s. w. Bd. 1, S. 401.

Uses.—That the use of pigment in the choroid coat is principally to render the eye achromatic, is sufficiently obvious from the principles of physics. We are ignorant of the uses which it serves in the walls of the blood-vessels in the amphibia.

BILE-PIGMENT.

Chemical Relations.

Properties.—This substance, like so many of the pigments, belongs to that vast group of bodies, whose chemical properties have never been thoroughly investigated; this is partly dependent on the circumstance that we can only procure it in very small quantity, and partly on its extreme instability, for not only does it occur in the animal organism under various modifications, but it is at once changed by the simplest chemical treatment. The most frequent modification which the primary substance of the bile-pigment in the higher animals appears to present, is the *brown pigment*, the *cholepyrrhin* of Berzelius, and the *biliphæin* of Simon. It occurs as a reddish brown, non-crystalline powder, devoid of taste and smell; it is insoluble in water, very slightly soluble in ether, and more so in alcohol, to which it communicates a distinct yellow tint; it is more soluble in caustic potash than in caustic ammonia, the alkaline solutions being at first of a clear yellow colour, but on exposure to the air gradually changing to a greenish brown tint. It is on this modification of the bile-pigment that the well-known changes of colour which occur in some of the animal fluids are dependent. The yellow solution of this pigment when gradually treated with *nitric acid* (and especially, according to Heintz*, when this reagent contains a little nitrous acid,) first becomes green, then blue (which, however, can hardly be detected in consequence of its rapid transition into violet,) and red; after a considerable period the red again passes into a yellow colour; by this time, however, the bile-pigment is entirely changed. On the addition of *hydrochloric acid* to a potash-solution, the pigment is precipitated with a green tint; this precipitate forms a red solution with nitric acid, and a green solution with the alkalies, and appears to be perfectly identical with the green modification of bile-pigment. The colouring matter contained in fresh bile is coloured green by acids; as Gmelin found that this coloration did not take place without the free access of oxygen, it is highly probable that most of these changes of colour are dependent on a gradual oxidation. Chlorine gas acts on this pigment in the same manner as nitric acid, but rather more rapidly; large quantities of chlorine completely bleach the pigment, and precipitate it in a white flocculent deposit.

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[*] Zeitschr. f. wiss. Zoologie. Bd. 1, S. 260-267.

This brown pigment has a strong tendency to combine with bases,—not merely with alkalies, but also with metallic oxides and alkaline earths. It forms insoluble compounds with the alkaline earths—a circumstance which has often led to the idea that this substance is insoluble.

The *green pigment*, the *biliverdin* of Berzelius, is a dark green amorphous substance, devoid of taste and smell, insoluble in water, slightly soluble in alcohol, but dissolving in ether with a red colour; it dissolves in fats, hydrochloric acid, and sulphuric acid with a green colour, and in acetic acid and the alkalies with a yellowish red tint. On exposure to heat, this body undergoes decomposition without fusing, and without giving off any appreciable quantity of ammonia, leaving a little charcoal. Berzelius regards this substance as perfectly identical with the chlorophyll of leaves, and believes that he has found all three modifications of this substance in different specimens of bile. This green pigment no longer undergoes changes of colour on the addition of nitric acid, although we occasionally meet with green bile-pigment still possessing this property. On treating bile-pigment with alkalies or acids, its properties are usually at once changed, partly on account of its entering into various combinations with these substances, and partly from the extreme facility with which it becomes decomposed.

Hence it is that the statements regarding the properties of this substance present such striking differences, as may be seen by a comparison of the writings of Berzelius[*], Scherer[†], Hein[‡], Platner[§], and others.

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* Müller's Arch. 1846, S. 399-405.

Berzelius also found in the bile a substance occurring in small reddish yellow crystals, soluble in alcohol, to which he has given the name of *bilifulvin.* I have obtained it in solution, but have never succeeded in isolating it in the solid state; singularly enough, I have often found it in the bile precipitated with neutral and basic acetate of lead; hence it appears either not to be precipitated by these metallic salts, or (which is more probable) to redissolve in an excess of the basic salt.

Composition.—With our present ignorance of bile-pigment in its pure unchanged state, it is not to be wondered at that its elementary composition is still unknown. Bile-pigment has been analysed both by Scherer and Hein, but it is obvious from their analyses that they have examined very different substances, and Scherer has especially shown that the pigment which he examined loses much carbon and hydrogen by the action of air, alkalies, and acids. From 7 to 9% of nitrogen has been found in bile-pigment.

Preparation.—Till recently the ordinary mode of preparing bile-pigment consisted in the extraction, by water and ether, of biliary calculi, consisting for the most part of this constituent; the residue thus obtained does not, however, generally possess the power of dissolving in alcohol, for (as Bramson[||] has very correctly shown, and as any unprejudiced observer may easily convince himself) it exists in a state of insoluble combination with lime, even in those concretions which for the most part consist of cholesterin.

The mode of investigation which Bramsom adopted, and which I have often repeated, appears to me to leave no doubt regarding the correctness of his views, which moreover receive further confirmation from the analyses of biliary concretions made by Schmid[¶] and Wackenroder.[**]

Berzelius prepares biliverdin from ox-gall by precipitating the alcoholic extract with chloride of barium; the precipitate is first washed with alcohol, and afterwards with water, and then decomposed with hydrochloric acid, which extracts the baryta; the fat is removed by ether from the residue, which is then dissolved in alcohol.

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[*] Lehrb. d. Ch. Bd. 9, S. 281-286.

[†] Ann. d. Ch. u. Pharm. Bd. 53, S. 377.

[‡] Journ. f. pr. Ch. Bd. 40, S. 47-56.

[§] Ann. d. Ch. u. Pharm. Bd. 51, S. 115.

[||] Zeitschr. f. rat. Med. Bd. 4, S. 193-208.

[¶] Arch. der Pharm. Bd. 41, S. 291-293.

[**] Ibid. S. 294-296.

Platner precipitates the bile-pigment by digesting the bile with hydrated protoxide of tin; the light green deposit which is formed, after being well washed with water, is shaken with spirit containing sulphuric acid, and filtered; the pigment is thrown down in the form of a green flocculent precipitate on the addition of water to the filtered green solution.

Scherer separated the bile-pigment from urine containing large quantities of it by means of chloride of barium, in the two following ways: he either decomposed the baryta-compound with carbonate of soda, threw down the pigment with hydrochloric acid from the soda-solution, and purified it by solution in alcohol containing ether, by washing with water, &c.; or the baryta-compound was extracted with alcohol containing hydrochloric acid, the solution evaporated, extracted with water, and then treated in the manner above described.

Tests.—Unless the amount of bile-pigment in a fluid be not too minute, nitric acid, especially if it contain a little nitrous acid, gives the very characteristic play of colours which we have already described. When, however, the colouring matter is present in small quantity, or when it has already undergone a partial modification, nitric acid often fails to give any appreciable reaction. Schwertfeger's* method in such cases is to precipitate the fluid with basic acetate of lead, and to extract the precipitate with alcohol containing sulphuric acid: if any of the pigment be present, the alcohol assumes a green tint. Heller† recommends that a little soluble albumen should be added to the fluid to be examined (unless, indeed, it be already albuminous), which must be precipitated by an excess of nitric acid; if any pigment be contained in the fluid, it will communicate a bluish or greenish blue tint to the coagulated albumen. Heller observes that if ammonia be carefully poured upon urine which contains unchanged bile-pigment, the surface of the fluid assumes a red colour.

Physiological Relations.

Occurrence.—Bile-pigment usually occurs in fresh bile in a state of solution; often, however, it is in a state of suspension. It almost always constitutes the nuclei of gall-stones; and we sometimes find ramifying nodular concretions in the gall-bladder and in the biliary ducts, consisting almost entirely of bile-pigment. This pigment is found, not only in the bile of man and of the ox, but also in that of other carnivorous and herbivorous animals; it presents, however, the most varied modifications, as we find from the difference of colour exhibited by the bile not only of different genera but even of different individuals of the same species ; thus, the bile of a dog is of a yellowish brown tint, that of the ox is brownish green, while that of birds, fishes, and amphibia is usually of an emerald green.

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* Jahrb. f. prakt. Pharm. Bd. 9, S. 375.

† Arch. f. Chem. u. Mikrosk. Bd. 2, S. 95.

The bile-pigment which mixes with the *contents of the intestines* becomes very rapidly modified, and ceases to present the ordinary reaction with nitric acid; the change which it here very rapidly undergoes, appears to be the same which we can induce artificially by nitric acid. It is in this form that it occurs in the *solid excrements,* unless when diarrhœa is present, in which case unchanged pigment is found in the alvine dejections. It is only rarely that the excrements assume a green tint from the green modification of the pigment; the green coloration more frequently depending on an admixture of partially decomposed blood. Bile-pigment is never entirely absent in the excrements except in the rare cases of icterus, which are accompanied with a complete stoppage of the biliary secretion.

Bile-pigment occurs in the *blood* and in *serous fluids* in all forms of icterus; sometimes however it is absent, or at all events, cannot be detected in the blood in certain forms of inflammation, while cholic acid or its conjugated acids may be recognised; the converse case, namely, the presence of bile-pigment and the absence of cholic acid in the blood is, however, more frequently observed. We shall return to this subject in the second volume.

In diseases the bile-pigment is especially deposited in the fluids of the cellular tissue, in the aqueous humour, the vitreous humour, the crystalline lens, and above all in the sclerotic; cases have even occurred in which the saliva and the sweat have been coloured yellow; sometimes the organism may so long endure this impure condition of the blood, that the pigment saturates even the cartilages, ligaments, and bones,* and may actually be recognised in the nerves.

Scherer† often discovered decided traces of bile-pigment in the *urine* of healthy persons, especially during the hot months. In disturbances of the function of the liver this pigment very frequently presents itself in the urine, and may usually be recognised by a brownish red or cinnamon brown, dark colour, which sometimes, if the urine be allowed to stand till it become acid (Scherer), passes into a dark green tint. Sometimes, however, it is also absent in this fluid while other biliary constituents are present in it. Occasionally, in perfect suppression of the biliary secretion—as for instance in true granular liver, when the urine throws down an intense scarlet sediment—no trace either of bile-pigment or of cholic acid can be detected.

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* Kerkring, Spicil. anat. obs. 57, p. 118.

† Ann. d. Ch. u. Pharm. Bd. 57, S. 181-195.

Origin.—As we are still unable to obtain an empirical formula for the composition of bile-pigment, chemistry affords us no information regarding the origin of this substance. The opinion has certainly long been advanced that bile-pigment was formed from hæmatin, in consequence of the greenish shades of colour which extravasated blood usually exhibits, as for instance under the skin after contusions, in the sputa of patients with pneumonia, and sometimes in typhous stools. However plausible this view may appear when we examine the blood-corpuscles of portal blood and find the colouring matter essentially changed in them, yet physiological facts are still wanting to support it. Virchow,* by his physiological investigations, has with much ingenuity pointed out the way which the chemist must proceed in order to decide the question in reference to this pigment. He was the first to draw attention to the red crystals which are found within the animal organism and which evidently arise from stagnating bile, and to show that in their reactions they take an intermediate place between hæmatoidin and bile-pigment, forming a transition stage between these two pigments.

Uses.—Whether the bile-pigment takes any part in the process of digestion, and what are its uses in the intestinal canal, are questions which for the present must remain altogether undecided. The fact that it undergoes so decided an alteration in the intestinal canal leads us teleologically to infer that it fulfils some special object.

These crystals, which are possibly identical with the bilifulvin found by Berzelius in bile which had already undergone change (Fel tauri inspissatum), have been found on the wall of echinococcus-sacs, which, in consequence of ruptures and partial resorption of the walls, communicated with the biliary ducts.

The facts now in our possession seem to indicate that the liver is not the part of the organism in which the bile-pigment is formed; we shall, however, discuss this question in the second volume, when treating generally of the origin of the bile.

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* Arch. f. pathol. Anat. u. s. w. Bd. 1, S. 427-431.

URINE-PIGMENT.

Considered either in a chemical or in a physiological point of view, there is scarcely any substance in the whole range of physiological chemistry regarding which our knowledge is in so unsatisfactory a state as the urine-pigment.

Experiments have often been commenced upon this substance, but the difficulties which present themselves in the investigation are so numerous that most experimentalists have soon resigned it, and directed their labours to some more productive department of chemistry. It unfortunately happens that no certain chemical differences can be detected between urines presenting the most striking difference of colour to the eye of the clinical physician.

The difficulties of this investigation are dependent on the following circumstances.

The amount of this substance in the urine is extremely minute; a very small quantity of the pigment giving a colour to an extremely large amount of other matters.

It begins to decompose even during the most cautious evaporation of the urine: to be convinced on this point we need only compare urine concentrated by evaporation, with a specimen from which a great part of the water has been removed by congelation.

Even on exposure to the air, or under the air pump, the decomposition of this substance commences.

Like many other pigments, it adheres tenaciously to other substances, sharing their solubility or insolubility.

Besides the pigment, there are other substances in the urine which have the same degree of solubility, which do not crystallise, and are not volatile; as they neither combine in definite proportions with other bodies, nor differ in solubility from the pigment, they cannot be separated from it.

The pigment occurs in the urine under various modifications, on which are dependent the different tints presented by morbid urine and its sediments.

Finally, this pigment is very readily acted on by chemical reagents, especially by acids and alkalies.

Scherer's* investigations on this subject especially show that this

* Ann. d. Ch. u. Pharm. Bd. 57, S. 180, 195.

pigment is in a state of constant change, that it is decomposed by neutral and basic acetate of lead into two substances, differing in their respective amounts of carbon and hydrogen; and that in a healthy condition of the system it is poorer in these two elements than when there are diseased conditions of the organism impeding the pulmonary or cutaneous transpiration, or the secretion of bile. That portion of the colouring matter which is richest in carbon, forms, as has been found by Scherer and Heller,* a dark blue powder, which when dried, possesses a coppery lustre similar to indigo, and dissolves in alcohol with a splendid purple colour. This latter variety of pigment is especially frequent in Bright's disease. Heller distinguishes three such pigments, *uroxanthin*, *uroglaucin*, and *urrhodin*.

It is a matter of common experience in science generally, and in chemistry more particularly, that the most circumstantial details are given in reference to the more obscure and less investigated departments, and that deficiencies of knowledge are concealed by an enumeration of unconnected or inaccurately observed facts, or by the most illogical deductions. For ourselves, however, we prefer to confess our ignorance, and to spare our readers from the accumulation of individual features which are incapable of affording a characteristic representation of the subject we would illustrate. Chemists still reckon the urine-pigments amongst what they term extractive matters, and may be said by this arrangement to make a candid avowal of their ignorance in reference to these substances.

Those who may be desirous of attempting to elucidate this obscure subject experimentally, may derive considerable advantage from the study of the older writings of Prout, Berzelius, and Duvernoy, and the more recent memoirs of Heller and Scherer.

EXTRACTIVE MATTERS.

The above observations on the colouring or extractive matters of the urine, lead us to the consideration of extractive matters in general, and of those of the blood in particular. The term *extractive matter* is applied by chemists to those bodies which, whether they are chemically produced, or exist preformed in an animal fluid, exhibit few distinguishing properties (that is to say, are uncrystallisable, incapable of entering into any crystallisable or stoichiometrically constituted combinations with other substances, are not volatile at a certain degree of temperature, &c.,) and cannot therefore be separated, or exhibited in a pure state. Modern science has indeed made considerable advance, by learning on the one hand to avoid as far as possible the formation of such substances, and on the other, to separate some of them, and render them more accessible to accurate chemical investigation. We will here observe that substances such as albuminate of soda, Mulder's binoxide and teroxide of protein, creatine, the inosates, &c., have been reckoned among the extractive matters; and as many better known substances (as urate of soda, hippurate of soda, and others) are impeded in their crystallisation, and are enveloped or concealed as it were by the extractive matters, they also have been embraced under the same head, and have likewise been regarded in the light of extractive matters, and have been calculated as such in analyses. When we consider that the matters circulating in the blood are, on physiological grounds, engaged in an almost constant metamorphosis, we shall easily comprehend the difficulties that beset the chemist in his attempt to seize them at any definite stage of their metamorphosis, especially as they only circulate through the blood in small quantities for the purpose of being deposited in some tissue, or of being eliminated from the organism by the organs of excretion.

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* Arch. f. Chem. u. Mikrosk. Bd. 2, S. 161 173.

The extractive matters must, therefore, be likewise regarded as important factors in the metamorphosis of animal tissue. In accordance with the views of Berzelius, these bodies were considered for the most part as products of the metamorphosis of tissues which, having become unfitted for further purposes, after fulfilling their function, are elaborated in the blood in the better known form of excrementitious matters. But to regard these substances as of a purely excrementitious nature, was taking too circumscribed a view of their importance. Since the blood contains the products of the metamorphosis of the tissues no less than the elements necessary for their formation, it is not only possible but probable that plastic and useful matters, as well as the products of regressive formation, may have been comprehended under the head of extractive matters; for, as we have already observed (p. 27,) the idea of the progressive and regressive metamorphosis of matter cannot be followed through an unbroken series of sequences.

Albuminate of soda, fibrin itself, and Mulder's protein-oxides, cannot assuredly be regarded in the light of excrementitious substances, but must rather be considered to constitute the transitions from albuminous to gelatigenous substances.

When we reflect that the different stages of metamorphosis of such non-nitrogenous bodies as the fats and carbo-hydrates increase the number of the extractive matters, it seems worthy of notice that their sum in the blood should not be greater than we generally find it to be. But this circumstance proves that very small quantities of the substances which must necessarily occur in the blood, appear simultaneously; and hence the difficulties of the inquiry are considerably increased. The reasons why we are thus unfortunately constrained to continue the use of the term extractive matters, are sufficiently clear, but yet we cannot refrain from expressing our surprise that, considering the present condition of our science in this respect, chemists can venture to speak of different crases of the blood, or attempt to make them serve as the foundation of a presumed exact humoral pathology.

NITROGENOUS HISTOGENETIC SUBSTANCES.

The substances belonging to this class present, like the fats and carbo-hydrates, such great similarities in their composition, and in their most essential properties, that chemists, even if they were unacquainted with their occurrence in the animal body, and with their great physiological importance, would naturally have placed them in one group, seeing that the following properties are common to all of them.

In the dried state they occur in a solid mass, or in powder, or form gelatinous, brittle, translucent plates; when moist they are either translucent and yellowish, opaque and white, solid and elastic, soft, tough, and adhesive, or, finally, jelly-like and slippery. All these substances are uncrystallisable, and, unless when an intermixture of other substances is present, are devoid of taste and smell. By far the greater number of them are insoluble in water, and the few which are soluble in it can readily undergo a conversion into a modification insoluble in that fluid; although their physical properties are essentially dependent on and modified by water, and although when dried they condense water with very great rapidity from the atmosphere (and are therefore highly hygroscopic), yet they show little tendency to form definite hydrates, that is to say, chemical combinations with water; they are insoluble in alcohol, ether, and in all neutral menstrua; none of them are volatile: many of them certainly fuse when heated, but not until decomposition has already commenced; at a higher temperature, after the loss of water, they develope a large number of nitrogenous and non-nitrogenous, basic and neutral products, in addition to ammonia, evolving at the same time an unpleasant odour, which is usually compared to that of burnt horn.

A very large number of the substances belonging to this group dissolve unchanged in *acetic* and other organic acids, as well as in common phosphoric acid; and also partially in other mineral acids in a state of extreme dilution. On the other hand, almost all of them are decomposed by *concentrated mineral acids;* many of them swell and assume a gelatinous appearance in *sulphuric* and in *hydrochloric* acid; after prolonged digestion, they form, together with ammoniacal salts, brown humus-like substances, which consist mainly of leucine and tyrosine, (see pp. 142-3,) and a crystallisable stinking volatile substance, which has not yet been accurately investigated. All, more especially when they are heated, assume a more or less intense yellow colour when treated with *concentrated nitric acid.*

They are all metamorphosed by prolonged *boiling with water;* and the metamorphoses they thus experience from being heated with water, have led to their classification into *albuminous* and *gelatigenous substances.*

The alterations experienced by these bodies from the action of *oxidising substances,* as for instance, chromic acid or manganese and sulphuric acid, have been most accurately studied during the last few years by Schlieper* and Guckelberger;† and it is worthy of remark that the non-nitrogenous products of this process of oxidation belong to the butyric acid group, embracing all the acids from formic to caproic acid and their aldehydes; besides these we must also reckon benzoic acid and hydride of benzoyl; but excepting ammonia and hydrocyanic acid, there are only very few nitrogenous products, namely the nitriles of some of the acids of the butyric acid group.

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* Ann. d. Ch. u. Pharm. Bd. 59, S. 1-32.

† Ibid. Bd. 64, S. 39-100.

Some few of these substances are dissolved by the *caustic fixed alkalies* in such a manner, that they can be again precipitated by acids in a perfectly unchanged condition; but the majority can only be dissolved in a concentrated alkaline solution, and with the continued application of heat, by means of which they become perfectly decomposed. Since the greater number of the bodies belonging to this group contain sulphur in addition to the ordinary elements of organic substances, the first effect produced by the action of heated dilute alkaline solutions is the abstraction of the sulphur by the formation of liver of sulphur and of alkaline hyposulphites. There is always a development of ammonia, although this is most considerable when concentrated alkaline solutions are used; carbonic and formic acids volatilise with the ammonia, while new bodies appear in the decoction, having either an acid, or a nitrogenous basic, or indifferent character, as for instance, leucine, glycine, protide, &c. If these substances be mixed with alkalies and gently fused, there will appear a large quantity of cyanide of potassium, leucine, tyrosine, &c., besides the ordinary products of the dry distillation of nitrogenous substances.

It is worthy of remark that these substances have the property of being reduced to the humid condition of *putrefaction* without any apparent or recognisable agency of other matters, and solely by the influence of atmospheric agents. While it is proved that other organic substances admitting of ready decomposition, as, for instance, urea, are not decomposed by the atmosphere even under the most favourable conditions, if they are in a chemically pure condition, the connexion of the elementary molecules of these bodies is so easily disturbed by the most ordinary atmospheric influences, that in the presence of water, and at an ordinary temperature, they begin to decompose in the course of a few hours, or, at all events, in a day or two. The period during which they can resist these influences, that is to say, the commencement of decomposition, depends greatly on the state of cohesion in which the molecules occur. The substances deposited in comparatively dense and insoluble masses in the animal tissues, pass far more slowly into a state of putrefaction than the more finely distributed substances, or those which are dissolved in water. The substance of the tendons putrefies less rapidly than cellular tissue and coagulated albumen, and the latter less rapidly than soluble albumen. The products of the putrefaction of these substances have not yet been sufficiently investigated; but among them are always to be found carbonate, butyrate, and valerianate of ammonia, sulphide of ammonium, leucine, and tyrosine.

It is further worthy of observation that all histogenetic substances are *invariably accompanied with fats, alkalies, and salts of lime,* from which it is impossible or very difficult to separate them without decomposition. It is not improbable that in the majority a portion of these admixtures is chemically combined with them; and although but few of these chemical combinations, as that of casein and phosphate of lime, admit of actual demonstration, many chemists are disposed to regard a part of these adhering matters as chemically combined, since the most ordinary indifferent solvents are unable to separate them, while the more powerful agents exert a decomposing or at least a metamorphic action on the main substance; and this applies more especially to the mineral substances accompanying these matters. Rose's investigations* regarding the mineral substances, have recently given greater weight to the idea that they may in part at least be combined in a non-oxidised condition with nitrogenous bodies, as has long been conjectured, in accordance with Mulder's views, to be the case with the sulphur, and in part also with the phosphorus of these substances. Rose has advanced very satisfactory grounds for believing that a portion of the alkalies and alkaline earths is contained in these matters in a metallic condition, and combined with radicals containing phosphorus and sulphur. We purpose, however, reverting to this subject under the head of "the mineral substances of the animal body."

It may easily be inferred from the abovenamed properties, that *it is extremely difficult or perhaps quite impossible to exhibit these bodies in a chemically pure condition.*

By their not crystallising, and by their not volatilising without decomposition, we are deprived of two most important means of readily isolating them from other substances; while the readiness with which they are decomposed, has hitherto prevented us from ascertaining which of the above mineral substances are chemically combined, and which are simply mixed with them. This refers specially to the soluble bodies of this class, as albumen, casein, &c., none of which have as yet been exhibited in a chemically pure soluble form. We are still more in doubt in reference to the insoluble substances deposited in the tissues; for even if we succeed (which we rarely can) in extracting from them all mineral substances, we yet have no guarantee that there is only one simple, organic substance deposited in the remaining mass of tissue; and both microscopic and microscopico-chemical investigations have rendered it probable that several chemical substances are mechanically deposited by the side of one another in many of the animal tissues, as quartz, mica, and feldspar, occur together in granite, and cellulose and the incrusting matter, in vegetable cellular tissue. It is often impossible to determine whether, after treating animal tissues with the more powerful solvents, the dissolved matter was originally only mixed with the undissolved, or whether it must be regarded as the product of decomposition of a body having a more complicated composition.

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* Ber. d. Akad. d. Wiss. zu Berlin. Decbr. 1848, S. 455-462.

We might perhaps succeed in exhibiting these substances in a chemically pure condition, and in acquiring a more accurate knowledge of their chemical constitution, if they could only be united with other substances in definite proportions, and admitted, if possible, of a single neutral combination; but such, unfortunately, in very few instances is the case. Many, it is true, obviously enter into chemical combination with alkalies, with the oxides of heavy metals, and even with acids, but as these combinations are mixed with other bodies and other compounds, we are hindered from establishing by analysis any definite relation between any two of these substances. Moreover, putting out of the question the alkaline and earthy salts that are blended with them, we find that no definite conclusions can be formed from the combinations of such animal matters with oxide of lead; for this oxide (which, with oxide of silver, we prefer to the other metallic oxides, since it almost always forms anhydrous compounds with organic substances, or compounds that can be readily deprived of their water) is found to combine with these bodies in more than one proportion; these compounds are then simultaneously formed, and cannot be separated from one another. The analysis exhibits more or less oxide of lead, according as the neutral compound is mixed with more or less of the basic compound. Hence we can readily understand the cause why chemists have succeeded in so few instances in determining with any certainty the saturating capacity and the atomic weights of these animal substances.

In the *arrangement* of these bodies we are again compelled to have recourse to a physiological principle of classification, which is the more admissible from the circumstance that chemistry here affords us no assistance. Our deficient knowledge regarding the chemical properties of the bodies included in this class, does not enable us to establish a purely chemical basis on which to ground their arrangement. But physiology so far aids us, that it indicates which of these substances are to be regarded as original and protogenic in the animal body, and which are to be regarded as originating from these by a zoo-chemical process, and constituting their derivatives. The protogens or aborigines of these substances, which are, in part, found in the embryo, bear so striking a resemblance to one another, that chemists have discovered only very slight, fluctuating, and often merely relative differences between them. We cannot wonder, therefore, that chemists should have conjectured that these, which had previously been termed *albuminous bodies*, possessed one common radical.

Mulder believed that he had discovered this radical, which, from its great importance, he designated as *protein*, whilst he regarded the ordinary albuminous substances as combinations of this protein with sulphur and phosphorus, or simply with sulphur, and therefore called them *protein-compounds*. Although great doubt has recently been thrown on Mulder's view of protein and its compounds, we yet retain these names for the sake of facilitating our comprehension and general examination of these combinations. We purpose considering the protein-compounds or albuminous bodies in the first group of histogenetic substances. As, however, physiological chemistry has shown, with great appearance of probability, that all other nitrogenous animal substances are derived from these protein-compounds, we will comprise, under the second group, all those more generally diffused substances of the animal body, which may be regarded as proximate or remote derivatives of these compounds.

PROTEIN-COMPOUNDS.

The bodies belonging to this group occur not only in animals, but also to a certain extent in plants. They were for a long time regarded as merely different isomeric modifications of one and the same compound; but subsequently, as already observed, they have been considered by Mulder to be combinations of one and the same atomic group with sulphur and phosphorus. The difficulty of solving this question will be made apparent on comparing the properties of these substances, and considering the observations already made (at pp. 29–30) on the determination of the atomic weights. It must rather excite our surprise that chemists should have hazarded any theory of their composition, than that nothing positive should as yet have been ascertained regarding their composition and mutual relations. Although we have the most accurate analyses of the protein-compounds, it is impossible to form any decisive conclusion regarding their internal constitution; for although the exactness of Mulder's analyses is undoubted, their accuracy must yet be only commensurate with the present comparatively imperfect state of analytical chemistry; that is to say, the empirical results of the analyses of these bodies do not admit of our deciding with scientific certainty on their composition. Hence a formula deduced from these analyses must be simply hypothetical, since several formulæ may frequently be derived with equal correctness from one and the same analysis. In making choice of one of these formulæ we must therefore adopt that which appears to guide us in the best direction, bearing in mind that we have to deal with hypotheses only, and not with facts.

Keeping this consideration in view, we have, in the following remarks, adhered to Mulder's recent hypothesis, in accordance with which albuminous substances are regarded as combinations of a purely hypothetical substance, incapable of being exhibited in an isolated form, with different quantities of sulphamide and phosphamide. We only follow this hypothesis, because from the want of a safer guide, it seems the best adapted to lead us in our advance through this obscure department.

The following properties are common to all the protein-compounds. Most of them occur in two conditions, namely in a soluble and in an insoluble or scarcely soluble state; in the former condition, we find them naturally existing in the animal fluids, while they are principally obtained in the latter form by boiling. The soluble modification forms in a dry condition a faint yellow, translucent, friable mass, having no smell or peculiar taste; it dissolves in water, but is insoluble in alcohol and ether; it is precipitated by alcohol from the aqueous solution, after which it is usually insoluble in water; the aqueous solution may have either a slightly alkaline or a slightly acid reaction, which depends, however, more on the alkali or acid mixed with it than on the substance itself. The aqueous solution is precipitated by most metallic salts, and the precipitate generally contains the acid and base of the salt employed in addition to the protein-compound. The greater number cannot be precipitated from their aqueous solution by alkalies or by most of the vegetable acids, but they are precipitated by mineral acids (with the exception of ordinary phosphoric acid) and by the tannic acids.

Most of them are transformed into their insoluble state by boiling, some by acetic acid, and almost all by the mineral acids; with the latter they usually form compounds soluble in pure water but insoluble in water to which an acid has been added, and incapable of being restored to the soluble modification by saturating the acid with a base. The protein-compounds, when precipitated by salts, usually assume the insoluble form.

The insoluble compounds, when dried, are white and pulverisable; when newly precipitated they are usually of a snow-white colour, flocculent or in small clots, or else tough and gelatinous, without taste or smell, without reaction on vegetable colours, and insoluble in water, alcohol, ether, and all indifferent menstrua; they are all more or less readily dissolved by *alkalies*, from which they can be precipitated by mere neutralisation with acids. They behave very differently towards different *acids;* they are dissolved by concentrated *acetic acid* and other organic acids, as well as by ordinary phosphoric acid, and are precipitated *from these solutions by yellow as well as red prussiate of potash.* They do not dissolve in moderately concentrated mineral acids, although they combine with them, and these compounds have the property of being insoluble in water to which an acid has been added, although they dissolve in pure water, after having first swelled and assumed a gelatinous appearance. They swell in the same manner in concentrated sulphuric acid, but they assume at the same time a brownish colour, and become decomposed. Their relation to *concentrated nitric* and hydrochloric acid is highly characteristic; the former acid giving them when heated a deep *lemon-coloured* tint, while *concentrated hydrochloric acid* causes them to assume a gradually increasing intensely *blue* colour, when exposed to a moderate warmth and to a sufficient supply of air. A fluid obtained by the solution of 1 part of mercury in 2 parts of nitric acid containing 4½ equivalents of water, forms the most delicate test for the protein-compounds, (Millon,*) whether they are dissolved in a fluid or simply interspersed in a tissue. The fluid, or the tissue that has been moistened with it, is then heated to from 60° to 100°, when an intense red colour is observed, which does not disappear either on prolonged boiling or exposure to the atmosphere.

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* Compt. rend. T. 27, p. 42-44.

The protein-compounds, when submitted to dry distillation, when allowed to putrefy, and when decomposed by oxidising agents, behave precisely in the manner of the histogenetic substances generally, which has been already described (pp. 322-3); giving rise to the above-named products of decomposition, although in different relations of quantity.

All protein-compounds contain *sulphur*, which can be very readily detected in these substances both in their natural state, and when boiled, either by heating them with a little alkali on silver foil (when a yellowishbrown spot of sulphide of silver will be formed,) or by boiling their alkaline solution for some time with strong acids, when sulphuretted hydrogen will be developed, or with acetate of lead, when sulphide of lead will be precipitated. It is, however, worthy of notice that the protein-compounds may contain sulphur under conditions in which its presence cannot be detected, as Mulder has shown, by the ordinary tests. These were the bodies which were at one time regarded by Mulder as protein, or the non-sulphurous constituents of albuminous matters, but he has subsequently discovered* that the substance formerly termed protein contains sulphur. On treating albuminous substances with a dilute solution of potash as prescribed for the preparation of this supposed protein, they lose the property of indicating the presence of sulphur by the ordinary tests. Mulder endeavours to explain this phenomenon by supposing that those compounds which yield a sulphur-reaction, contain sulphur combined with amide, and therefore as *sulphamide* H_2NS; and further, that on treating them with potash, 2 atoms of sulphamide by assimilating 2 atoms of water, are decomposed into ammonia which escapes, and also into hyposulphurous acid, which combines with the non-sulphurous atomic group to form those compounds which yield no sulphur-reaction on silver foil. It certainly is true that all these compounds on being digested with caustic fixed alkalies, develope ammonia, and that those yielding the sulphur-reaction contain more nitrogen than those which do not exhibit it. The assumption of the presence of sulphamide in these substances, must, however, still be regarded as a somewhat hazardous hypothesis, in the first place, because we are as yet wholly unacquainted with this sulphamide, whether in an isolated or combined state; secondly, because a combination of hyposulphurous acid with an organic, scarcely basic substance, is as unlooked for a phenomenon, as that it should not be separable by stronger acids from its combination with the protein;

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* Chem. Untersuch. übers. v. Völcker. H. 2, S. 179-272.

and lastly, because the hyposulphites yield a most evident sulphur-reaction when heated with organic substances on silver foil. Mulder in like manner assumes that the phosphorus contained in albumen, exists in the state of *phosphamide*, H_2NP, a purely hypothetical body, and totally different from Gerhardt's phosphamide, whose amide nature is moreover very doubtful. These are some of the grounds on which we have been led to regard Mulder's view as a mere scientific fiction. By subtracting the elements of hyposulphurous acid from the composition of those albuminous substances which do not yield the sulphur-reaction, and the elements of sulphamide from those yielding such a reaction, Mulder obtained a group of atoms of carbon, hydrogen, nitrogen, and oxygen, which in all these compounds exhibited perfectly identical relations, or only a slight increase of oxygen. This complex atomic group contained in 100 parts 54·7 of carbon, 6·8 of hydrogen, 14·2 of nitrogen, and 24·3 of oxygen. For this complex group Mulder has calculated the formula $C_{36}H_{25}N_4O_{10}+2HO$, which expresses, according to him, the true composition of the perfectly non-sulphurous protein.

The sulphur which is not detected by the above named reactions can only be discovered and quantitatively determined by the dry method; fusing the dry, organic substance with a mixture of alkaline nitrates and carbonates or caustic alkalies in a silver crucible till the fused mass becomes perfectly white, when the sulphuric acid which has been thus formed, can be determined from the residual saline mass.

ALBUMEN.

Chemical Relations.

Properties.—Albumen, the principal representative of the protein-compounds, is distinguished amongst these bodies by its occurrence in very different modifications, which are however not to be sought in a different arrangement of the atoms of this substance, that is to say, in a polymerism or metamerism, but depend alone on the substances mixed with it, as alkalies and salts. Hence the albumen of the blood differs in several points of view, not only from that of the hen's egg, and the latter from that of a dove's egg, but it is even found that the albumen of the blood differs in different persons, and that the albumen of the albuminous fluids of the same individual does not exhibit precisely similar reactions.

This is one of the causes that has given rise to the various and frequently contradictory statements abounding in chemical literature, in reference to the individual properties of albumen. Albumen obtained indiscriminately from various sources ought, therefore, not to be employed for qualitative chemical experiments, but we should first obtain albumen in a state of the greatest possible chemical purity, and we may then ascertain the modifications experienced in its properties and reactions by the admixture of different substances in different proportions; for striking differences are produced in albumen, not merely by the presence of another body, but by the different proportions in which it occurs. Scherer* and myself† were the first to investigate the properties of albumen in this point of view, but although we may have succeeded in elucidating some few individual points, no perfect and scientifically conclusive results have been attained; and notwithstanding our investigations, experiments have been subsequently made on albumen, containing various admixtures and taken at random from any sources. We shall in this place limit our remarks to the most important and general relations of albumen, lest, by introducing too many details, we should obscure and confuse our general survey. If even slight admixtures are capable of modifying the properties of albumen, we may readily comprehend how much more powerfully they may be affected by chemical changes, even if small, in the grouping or arrangement of the atoms. We know that some kinds of albumen vary in the quantity of sulphur they contain, and others again in their saturating capacity, but these are relations which require further investigation for their complete solution.

We purpose adhering to the old classification, and considering albumen in its soluble and coagulated states.

Soluble albumen, dried in the air, forms a pale yellowish, translucent mass, which may be easily triturated and reduced to a white powder. The specific weight of the albumen of the hen's egg, from which the salts had not been removed, was found by C. Schmidt‡ to be 1·3144; after calculating for the elimination the salts, the density of pure albumen was found to be 1·2617. It becomes positively electric by friction, and is devoid of smell, taste, and reaction on vegetable colours. It swells in water, assuming a gelatinous appearance, does not dissolve freely in pure water, but very readily in water containing chloride of sodium or any alkaline salt. It is insoluble in alcohol and ether.

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* Ann. d. Ch. u. Pharm. Bd. 40, S. 1-65, and Untersuch. zu Pathol. S. 82 ff.

† Arch. f. physiol. Heilk. Bd. 1, S. 234.

‡ Ann. d. Ch. u. Pharm. Bd. 61, S. 156-167.

After being dried *in vacuo*, or at a temperature below 50°, it can be *heated* to 100° without passing into the insoluble condition; the aqueous solution, however, becomes turbid at 60°, coagulates perfectly at 63°, and separates in flakes at 75°. When excessively diluted, no turbidity can be perceived below 90°, and coagula will only separate after it has been boiled for a considerable time.

Albumen may be precipitated from an aqueous solution by diluted *alcohol;* the precipitate, however, is not coagulated; but when a large quantity of strong alcohol is added, it is converted into the insoluble or coagulated form. It behaves very differently towards *ether* free from spirit; it is generally asserted that the albumen of the serum of blood is not coagulated, while that of eggs, on the other hand, is coagulated by ether; but as this observation is not constant, this supposed variation may be dependent on the degree of concentration of the albuminous solution.

Fatty and volatile *oils* neither dissolve nor coagulate albumen. It is coagulated by *creosote* and *aniline*.

Albumen is converted into the insoluble state by most acids, but it is not precipitated by the mineral acids (except by tribasic phosphoric acid) unless when they are added in excess. The organic acids, with the exception of the tannic acids, do not precipitate albumen.

Alkalies do not precipitate albumen, but they convert it into the insoluble modification.

The greater number of the *metallic salts* precipitate albumen; the precipitate containing either a combination of a basic salt with albumen, or a mixture of two compounds, one of which consists of the acid of the salt and albumen, and the other of the base of the salt and albumen. The albumen generally passes into the insoluble state in these combinations.

Albumen is not usually found *isolated* in solution in the normal animal fluids, but in combination with a small proportion of *alkali*, whose quantity does not admit of exact determination on account of the salts which are also mixed with the albumen. In some experiments conducted by myself on the albumen of hens' eggs, I found that 1·58 parts of soda were directly combined with 100 parts of albumen, calculated as devoid of salts. This albumen has a slightly alkaline reaction, is more readily soluble in water than pure albumen, from which it differs mainly in the form in which it coagulates when the aqueous solution is heated (Scherer); for it does not separate in flakes like pure albumen, but forms a white, almost gelatinous mass, or simply gives rise, if the fluid is more or less diluted, to a milky or only whitish opalescent turbidity. The alkaline reaction of the fluid is more strongly marked after boiling, which proves that at least a portion of the alkali must be separated from the albumen on its coagulation. The liberated alkali combines with a small portion of the albumen to form albuminate of soda, which remains dissolved. This albumen, separated by coagulation, passes however, in part, through the filter, and very soon clogs its pores. On saturating the solution of albuminate of soda with acetic acid, or some other organic acid, it will coagulate on being heated, like pure albumen, into flakes that may be readily collected on the filter. An albuminous solution, after being thus neutralised, is rendered turbid when diluted with a large quantity of water (about twenty times its own volume); a large portion of the albumen, poor in salts and free from an alkali, being precipitated from the solution.

This phenomenon is dependent upon the circumstance that the albumen, freed from the alkali by acetic acid, is held in solution by the salts, which, however, when strongly diluted, lose their solvent power, and cause the gradual separation of the albumen.

On treating this albuminate of soda with dilute alcohol, there is a precipitation of albumen free from alkali and poor in salts; whilst another portion combined with more alkali remains in solution and represents the true albuminate of soda, which we are now going to consider. This precipitate dissolves only slightly in pure water, but readily in aqueous saline solutions.

A further addition of alkali to the normal albumen contained in the animal fluids gives rise to an essential difference in its properties. When the solution has been highly concentrated, it yields, on being heated, a translucent jelly, almost insoluble in water, and containing, according to my observations, 4·69 parts of potash or 3·14 of soda to 100 parts of albumen free from salts. On diluting the solution with water, it no longer yields this colourless jelly or any precipitate whatever, on being heated. The albumen even appears entirely to have lost its coagulability, but such is not the case, for when treated with an excess of alkali, it becomes converted into the coagulated state even without the application of heat; for if the solution be neutralised with some acid that does not ordinarily precipitate albumen, (as acetic acid, tartaric acid, or tribasic phosphoric acid), albumen is separated in a coagulated state. The solution of this true *alkaline albuminate* is distinguished by the circumstance that, on boiling, numerous vesicles are formed at the bottom of the vessel, which adhere so tenaciously as to impart a brown colour to this organic substance in process of formation; its surface also becomes covered on evaporation with a transparent film of coagulated albumen (Scherer), which has frequently caused this albuminate of soda in the animal fluids to be mistaken for casein. This alkaline solution yields, however, on boiling, a perfect coagulum in the form of flakes or masses, if any neutral alkaline salt (such as sulphate of soda, chloride of sodium, or hydrochlorate of ammonia) either in the form of a saturated solution, or in the dry state, has been added to it, previously to its being boiled.

Acids and *metallic salts* behave to these alkaline solutions of albumen, nearly in the same way as to those of pure albumen; but the quantity of the metallic salt which is added, often induces modifications, the newly formed albuminates being in some cases soluble and in others insoluble in an excess of the metallic salt or of the albuminate of soda. The greater number of these compounds are however soluble in alkalies.

Organic acids added in excess to albuminous solutions, behave in the same manner as alkalies added in excess, causing the albumen to remain dissolved on boiling; if, however, neutral alkaline salts, such as sulphate of soda, chloride of sodium, or hydrochlorate of ammonia be added to these solutions, the albumen separates on boiling into flakes or clots. Further, these acid solutions on being evaporated are covered with a membrane similar to that which is formed by casein in acid or alkaline milk.

Coagulated or *boiled albumen* possesses all the properties which we have already noticed as exhibited by the insoluble protein-compounds in general. We will, therefore, simply observe that the albumen in its transition from the soluble to the insoluble state, loses a portion of its sulphur; for sulphuretted hydrogen is developed in appreciable quantity: with acids it enters into combinations that are insoluble in water containing acids, but swell and assume a gelatinous form in pure water, before undergoing solution in it. It may be so perfectly combined with caustic alkalies, as to cause their alkaline reaction entirely to disappear. When heated with concentrated hydrochloric acid it dissolves and assumes a blue colour which inclines more to purple than is the case with any other of the protein-compounds. If albumen be boiled for a long time in water, atmospheric air being not excluded, it gradually dissolves, forming a non-gelatinising fluid which contains Mulder's[*] teroxide of protein. Finally, albumen when treated with strong oxidising agents, as for instance, chromate of potash and sulphuric acid, or binoxide of manganese and sulphuric acid, yields more acetic acid, benzoic acid, and hydride of benzoyl, and less valerianic acid, than the other protein-compounds.

Composition.—Albumen, after being coagulated and extracted with water, alcohol, and ether, has been so repeatedly analysed, that we shall rest satisfied with giving the mean results of five analyses made by Scherer,[†] and subjoining an analysis recently made by Mulder,[‡] and regarded by him as the most exact.

	Scherer.	Mulder.	Rüling.
Carbon	54·883	53·5	53·4
Hydrogen	7·035	7·0	7·0
Nitrogen	15·675	15·5	
Oxygen	22·365	22·0	
Sulphur		1·6	
Phosphorus		0·4	
	100·000	100·0	

Rüling[§] found in the albumen of the blood-serum (after subtracting the ash, in accordance with the mean of several experiments) 1·325% of sulphur, and in that of hens' eggs, 1·748%, while Mulder found on an average only 1·3% in the former, and 1·6% in the latter. Albumen always retains chloride of sodium with so much tenacity, that it is almost impossible to separate it by washing. The quantity of phosphate of lime which it contains is very remarkable, for, although variable, it usually amounts to about 1·6%. Mulder found from its combination with oxide of lead that the atomic weight of albumen is 22483·9, while from the oxide of silver compound he calculated it at 22190·2. For the reasons already advanced, (at p. 324) we are as yet unable to establish an empirical formula for albumen; but Mulder calculates, according to the above hypothesis, that the albumen of eggs is composed of 96·2% of protein, 3·2% of sulphamide, and 0·6% of phosphamide; and deduces from these numbers the very hypothetical formula, $20(C_{36}H_{25}N_4O_{10}.2HO)+8H_2NS+H_2NP$.

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[*] Ann. d. Ch. u. Pharm. Bd. 47, S. 300, and Bullet. de Néerlande, 1839, p. 404.

[†] Ann. d. Ch. u. Pharm. Bd 40, S. 36.

[‡] Scheik. Onderz. D. 3, p. 385.

[§] Ann. d. Ch. u. Pharm. Bd. 58, S. 310.

Combinations.—*Albumen-protein* contains, according to Mulder, 53·7% of carbon, 7·0% of hydrogen, 14·2% of nitrogen, 23·5% of oxygen, and 1·6% of sulphur. He prepares it by dissolving pure coagulated albumen in a solution containing from $\frac{1}{200}$th to $\frac{1}{400}$th of caustic potash, and exposing it for the space of an hour to a temperature of from 60° to 80°. The presence of sulphide of potassium in the solution may then be proved by the ordinary reagents. If we were at once to neutralise the fluid with acetic acid, there would be a danger that the precipitate would contain an admixture of sulphur, since, in addition to the sulphide of potassium, the fluid must also contain hyposulphite of potash, which on the addition of an acid, deposits sulphur, and forms sulphurous acid; this sulphurous acid again, as is well known, yields sulphur with the sulphuretted hydrogen which is developed; hence the fluid must be exposed to the air, and at the same time frequently stirred till it ceases to yield any further indication of the presence of sulphide of potassium; then, and not till then, we may precipitate the desired body by acetic acid.

When newly precipitated, albumen-protein is of a snow-white colour, and in the form of minute flakes; when dried, it assumes a pale yellow tint, is hard and brittle, swells in water into a jelly, but is insoluble in that fluid as well as in all indifferent menstrua, and for the rest behaves like coagulated albumen, with this exception only, that after the treatment with potash, it yields no indication of the presence of sulphur, either with the salts of lead or on silver foil.

Preparation.—We have already shown that soluble albumen cannot be obtained perfectly free from mineral constituents. The soluble modification may be obtained in the greatest purity by neutralising serum or the white of egg dissolved in water with a little acetic acid, and extracting with from 20 to 30 times the quantity of distilled water, or with dilute spirit. It is however usually prepared by evaporating the serum of the blood, or the white of egg in platinum vessels, either *in vacuo* or at a temperature not exceeding 50°, pulverising the yellow residue, and extracting it with ether, and finally with alcohol.

Coagulated albumen is obtained in a perfectly pure state by washing the precipitate yielded on the addition of hydrochloric acid to solutions of white of egg, with dilute hydrochloric acid, in order to remove the salts, and especially the phosphate of lime; by dissolving the hydrochlorate of albumen in pure water, and precipitating it with carbonate of ammonia. The precipitate is then dried, pulverised, and freed from fat by boiling alcohol and ether.

Wurtz* obtained a soluble albumen which, however, contained acetic acid, by treating the albumen of hens' eggs with basic acetate of lead, and removing the lead from the albumen by means of carbonic acid and sulphuretted hydrogen. This albumen reddens litmus.

Hruschauer† likewise obtained an albumen that reddened litmus by precipitating albumen with sulphuric acid. After being washed for a period of six weeks it reddened litmus; it was, however, free, from sulphuric acid.

Tests.—The presence of albumen is in general very easily shown, since the coagulability of a fluid by heat is usually regarded as a proof of its presence; but when we consider that several other substances (to be treated of in the sequel) likewise coagulate when boiled, we must not adopt this property of albumen as the sole means of its recognition, since, as has already been noticed, albumen under some relations either does not coagulate, or presents a scarcely perceptible turbidity. We have already indicated the methods by which the presence of albumen may be detected in very acid or very alkaline fluids; we either neutralise the fluid, or we treat it with a strongly saturated solution of hydrochlorate of ammonia, and then boil it. Many methods were formerly recommended for indicating the presence of albumen, especially when occurring only in very small quantities, among which we may particularly notice nitric acid, corrosive sublimate, bi-chromate of potash to which a small quantity of sulphuric acid has been added, and tannic acid; but these methods were only of value when applied in addition to the coagulation test, since the greater number of the protein-compounds are precipitated by them; they are, therefore, only regarded as conclusive when they yield reactions in a fluid in which no other protein-compound but albumen is generally found. Thus, for instance, when urine coagulates on being heated, and is likewise precipitated by nitric acid, corrosive sublimate, chromic acid, and other means, we entertain no doubt of the presence of albumen, although these tests yield the same reactions with most of the other protein-compounds. As, however, all these reagents collectively yield only a relative proof of the presence of albumen, we can trust but little to the evidence afforded by the mere coagulation of a fluid by heating, since animal fluids, as for instance urine, not unfrequently deposit, on heating, a dense, amorphous precipitate, showing no trace of albumen, and consisting only of phosphates. This is often the case when the urine is very slightly acid, but the precipitate may be distinguished from coagulated albumen by the addition of a mineral acid, which readily dissolves the earths, or by acidulating the urine, before boiling, with a little acetic acid, when no precipitate will any longer be obtained by boiling, if its presence were dependent on the earthy salts of the urine.

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* Compt. rend. T. 18, p. 700.

† Ann. d. Ch. u. Pharm. Bd. 46, S. 348.

In testing animal fluids, and especially those of a pathological nature, we must particularly observe the form in which the albumen coagulates, for on this, as has already been observed, numerous other relations depend; thus, a flocculent coagulum that admitted readily of being collected on the filter, would show that the albumen is not combined with an alkali, and that the latter must have been extracted from it by an acid, since, in the normal state all the albuminous fluids of the body contain albumen in combination with an alkali, and coagulate like milk, or in a white, opaque jelly. Again, if, on evaporation, an animal fluid from which the albumen has previously been removed by boiling, become covered with a thin, colourless membrane, we have no right to conclude, as is so frequently assumed, that casein is present, but simply that the fluid still contains sufficient alkali to prevent the ordinary coagulation of the albumen, and, in short, that although a portion of the albumen may have been removed by boiling, the fluid yet contains the so-called albuminate of soda or potash.

Morbid blood and exudations frequently contain pure albumen that has been dissolved merely by salts; from these fluids the greatest part of the albumen may be precipitated by dilution with large quantities of distilled water, first as a milky turbidity, and finally in flakes, as was first shown by Scherer.

In the determination of albumen it must always be recollected that we are unable to distinguish it from the similar protein-compounds with that scientific accuracy with which we are able to recognise most other organic substances. We may, indeed, indicate the differences presented by the individual reactions in similar substances; but albumen unfortunately occurs in several modifications, sometimes resembling one and sometimes another protein-compound, while neither the determination of the saturating capacity nor the elementary analyses of these bodies present any marked differences. Our determination of the albumen in an animal fluid must therefore at best exhibit only a relative certainty, and this is specially the case where we attempt to discover coagulated albumen; fortunately, however, it rarely or never occurs in this condition in the animal organism; and from what has already been said (at p. 328) in relation to the properties common to the coagulated protein-compounds, it must be apparent that in the present state of science it is useless to attempt drawing distinctions between them. Since the determination of the atomic weight and the elementary analysis are here unable to throw any light on the subject, we might be disposed to take the quantity of sulphur contained in a substance known to be a protein-compound (see p. 329) as a means of ascertaining its identity with coagulated albumen, fibrin, casein, &c., but it unfortunately happens that the quantity of sulphur contained in one and the same body, as for instance in albumen, is not constant. We must for the present relinquish all hope of distinguishing from one another the different coagulated protein-compounds of the animal body, and hence it is utterly absurd to enquire whether it be coagulated fibrin or albumen that exists in tubercles or in carcinoma; and yet this is a point which many adherents of the pathologico-anatomical school believe that they have satisfactorily settled without the aid of chemistry.

The method usually recommended for the *quantitative determination* of albumen in the animal fluids is simply to coagulate it by heat, to collect it on a filter, and to dry and weigh it. At the first glance this method seems to be highly practical, but as soon as we attempt to prosecute it, we find our course impeded by unexpected difficulties, unless we would rest content with such deficient and inexact analyses as unfortunately are too common in pathological chemistry. In the first place, it should be observed that the albumen commonly contained in slightly alkaline animal fluids cannot be regarded as capable of being collected on a filter after its coagulation; for while, on the one hand, some portion always passes through the filter in consequence of its gelatinous or milky character, the filter becomes on the other hand so quickly clogged with the coagulated albumen as to preclude the possibility of washing it out; or the fluid passes so slowly through the filter, that the albumen has time to putrefy. Those who suppose that these evils can be remedied by the use of linen or woollen materials as a filter, can have no idea of the degree of exactness required in a chemical analysis; and we cannot refrain from observing that the greater number of analyses of animal albumiminous fluids have been conducted in this manner, without any reference being made to these difficulties. Scherer is the only chemist who has directed attention to these obstacles in the way of an exact determination of the albumen, and given instructions regarding the manner in which they may be avoided. In order to determine with exactness the quantity of albumen in a weak alkaline fluid, we must neutralise or slightly acidulate it with dilute acetic acid previously to coagulating it; on the application of heat, the albumen will then coagulate in flakes, and may be both perfectly and rapidly collected on the filter, through which the fluid will pass in a state of perfect clearness. By this method another error incident to the ordinary mode of determining albumen is avoided, for as we have already observed, some alkali is always liberated on boiling any normal albuminous fluid, the fluid exhibiting a stronger alkaline reaction than it did before the boiling. This alkali forms, with a small quantity of albumen, the so-called alkaline albuminate, which, notwithstanding the boiling, remains perfectly dissolved. A portion of albumen must therefore be lost in the ordinary method, even when the coagulated albumen can be collected on a filter, for, as already observed, some of the albumen actually passes through the filter in a dissolved form. Scherer's method entirely obviates this cause of error; care must, however, be taken not to run into an opposite extreme in treating the albumen with too large a quantity of acetic acid, which would equally occasion a loss of the albumen by its solution in that fluid, and its consequent passage through the filter. Hydrochlorate of ammonia may be employed instead of acetic acid, but in this case a longer boiling is requisite, in order completely to precipitate the albumen from the fluid, and to render it capable of being collected on a filter. It depends entirely on the other steps of the analysis whether acetic acid or carbonate of ammonia be the best suited for the purpose.

This is, perhaps, the most fitting place for drawing attention to a point of the greatest importance in the *quantitative analysis of animal fluids*, as well as of organic parts; we allude to the manner of thoroughly drying substances to be weighed. The *thorough drying* of animal substances which are in themselves hygroscopic, or which contain admixtures of protein-compounds, extractive matters, &c., is by no means so easy as that of already dry substances, which, in order to be submitted to elementary analysis, have been exhibited in a perfectly pure state, and have been reduced to a pulverised condition before weighing. It is obvious that dessication must be effected with the same care as for an analysis with the combustion-tube, if we would not injure the result of the whole analysis; but the circumstance that the substances must here be weighed on filters (whose weight in a dry condition must be predetermined, and which are, moreover, hygroscopic), and that the substances to be weighed cannot be pulverised beforehand, very much increases the difficulty of our forming accurate determinations. Animal substances mostly form horn-like masses on heating, and become covered during dessication by a crust of dry matter, which is impervious to the water contained in the interior; hence it is frequently impossible to remove all the water contained in such substances without exposing them to a high temperature *in vacuo* and employing sulphuric acid. We must therefore, when it is possible, simultaneously employ high temperatures, air pumps, and hygroscopic bodies. As analytical chemistry indicates the numerous methods in which these three agents for the removal of water may be employed, we will here simply observe that the two following methods appear to us to constitute the most expeditious means of attaining a perfect dessication. We either heat a small and convenient sand-bath under the receiver of the air-pump to about 110°, and then place upon it the watch-glass or vessel on which the substance to be dried, together with its filter, has already been laid, and then place the sand-bath with the substance under the air-pump over sulphuric acid, and form a vacuum; or we place the substance to be weighed, together with its filter, in a weighed test-glass, which is surrounded by hot sand, and connected with a hand air-pump provided with a chloride of calcium tube, and the air is then abstracted exactly as in the manner directed by Liebig* in preparing bodies for elementary analyses. In either case the dessication should be continued as long as the substance is found to experience any loss of weight on being weighed. If the air-pump be dispensed with, and the drying be conducted solely by means of heat, as, for instance, by Rammelsberg's† or Liebig's‡ admirable air-bath, the temperature must first be raised to 110° or 115°, and the substance then allowed to cool *in vacuo*, for if this precaution were not adopted, the filter and the animal substance would, during their cooling, abstract water from the air, and thus increase in weight. The method proposed by Becquerel and Rodier for weighing substances, while still hot, seems even less to be relied on; for it is well known that by the heating of one of the scales of the balance, the rising current of air renders the substance to be weighed apparently lighter, and analytical chemistry shows us that hygroscopic substances, after being dried at a high temperature, must be cooled in a closed space over sulphuric acid before their weight can be ascertained with certainty. It is therefore here even more necessary than in the preceding method to repeat the process of weighing, until it yield a constant result.

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* Handwörterb. d. Chemie. Bd. 1, S. 360.

† Anleit. zur quant. min. Analyse. S. 50.

‡ Anleit. zur quant. chem. Analyse. S. 37.

When we consider that all the results of the analysis of organic bodies are entirely dependent on the completeness of the drying process, it is obvious that we can attach very little certainty to many of the published analyses of pathological products. Becquerel and Rodier, who, next to Scherer, have undoubtedly instituted the best analyses of morbid blood, deem it necessary to observe, as something worthy of special notice, that they have devoted the same attention to the quantitative analysis of the blood that is required for an elementary analysis; although we do not see any reason why less exactness is allowable in the far less controllable analyses of animal fluids, than in elementary analyses. In every analysis, but especially in organic analyses, the utmost care is demanded on the part of the experimenter; and where this is not afforded, the labour will result in nothing better than a loss of time and trouble, and a detriment to science. Indeed most of the analyses made in the department of pathological chemistry have been conducted by chemical *dilettanti*, who deluded themselves with the false idea that they were enriching science, and contributing to the establishment of exact medicine by their approximative estimates. It were better for the cause of science, had it never been weighed down by the unprofitable and crude burden of these analyses.

Physiological Relations.

Occurrence.—Albumen occurs in all those animal substances which supply the whole body, or individual parts of it, with the materials necessary for nutrition and the renovation of effete matters. Hence albumen is a principal constituent of the blood, the lymph, and chyle, as well as of all serous fluids. It also occurs in the fluids of the cellular tissue, in the white of egg, in the Graafian vesicles, &c. It is especially worthy of notice, however, that it is only in the uncoagulated state that albumen is found these parts; for, as we have already observed, it would be an impossibility, scientifically considered, to distinguish coagulated albumen from other insoluble protein-compouds in the animal body.

As we purpose in the second volume entering fully into the quantitative relations of the albumen in the *blood*, it will be sufficient here to observe, that the recent investigations of Becquerel and Rodier,* with the older ones of Lecanu,† Denis,‡ Simon, Nasse, and others, are tolerably agreed in stating that the quantity of albumen in normal blood fluctuates between 6·3 and 7·1% and in normal blood-serum between 7·9 and 9·8%; Scherer's§ is undoubtedly the best method that has yet been proposed for the analysis of the blood, which, according to his results, contains in healthy men from 6·3 to 7·0% of albumen. Nasse‖ and Poggiale¶ found on an average less albumen in the blood of most animals than in that of man, the highest quantity being 6·7%. The blood of men appears from the concurrent observations of experimentalists to contain rather less albumen than that of women.

The *chyle* contains less albumen than the blood, but the quantity is variable, as may readily be conjectured from the nature of this fluid; according to Nasse** it averages from 3 to 6%.

Marchand and Colberg†† found only 0·434% of albumen in human *lymph*, while in that of horses Nasse‡‡ found only 0·391%, including some fibrin, and Schlossberger and Geiger§§ only 0·62%.

The *white of hens' eggs* contains, according to Berzelius,‖‖ from 12 to 13·8% of albumen.

The *serous fluids* of the animal body, physiological as well as pathological, contain much less albumen than the serum of the blood, as indeed might be inferred *á priori* from their density; they are however never wholly free from it.

The *animal tissues* are almost all surrounded by albuminous fluid; but the large quantity of albumen found in many of these tissues depends upon the numerous capillaries by which they are intersected; as we specially observe in such organs as the liver, kidneys, brain, and muscles.

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* Gaz. méd. 3 Ser., T. 1, p. 503, &c.

† Etudes chim. sur le sang hum. Paris, 1837.

‡ Arch. gen. de Méd. 3 Sér. T. 1, p. 171.

§ Haeser's Archiv. Bd. 10, S. 191.

‖ Journ. f. pr. Chem. Bd. 28, S. 146.

¶ Compt. rend. T. 25, pp. 198-201.

** Handwörterb. d. Physiol. Bd. 1, S. 233.

†† Pogg. Ann. Bd. 43, S. 625-628.

‡‡ Simon's Beitr. z. phys. u. pathol. Chem. Bd. 1, S. 449-455.

§§ Arch. f. physiol. Heilk. Bd. 5, S. 391-396.

‖‖ Lehrb. d. Chem. Bd. 9, S. 650.

In the normal condition no albumen seems to pass into the *secretions*, as for instance the saliva, gastric juice, bile, mucus, &c., for although they do indeed exhibit traces of protein-compounds, these latter differ from ordinary albumen. The pancreatic juice contains, however, in its normal state a substance extremely similar to albumen, which coagulates on being heated, and perfectly solidifies the fluid (as in the white of hens' eggs). This substance may, however, occur in any of these fluids in morbid conditions of the secreting organ; and Jul. Vogel* has especially shown that the mucous membranes may secrete albumen in addition to the ordinary mucus-corpuscles, when abnormally excited; (hence the presence of albumen in a fluid resembling pus is no evidence of the presence of true pus, or rather of a suppurating surface.)

Bernard† found that the albuminous substance of the pancreatic juice exhibited the same behaviour in reference to acids, metallic salts, and to heat, as ordinary albumen, and that it was not coagulated by acetic or lactic acid. Bernard instances as a characteristic difference, that the substance of the pancreatic juice is soluble in water after its precipitation by alcohol, but this as we have already observed, is likewise the case with albumen when dilute alcohol is used. Concretions taken from the pancreatic duct, and for which I am indebted to the kindness of Professor Hasse, dissolved almost entirely in water and exhibited the ordinary reactions of albumen.

Mack,‡ Vogt, and Scherer,§ have found albumen in the *liquor amnii*, and the two latter enquirers ascertained from their observations that the amniotic fluid is richer in albumen in the earlier than in the later periods of fœtal life.

Vogt found in the fluid of a fœtus at the fourth month 10·77%, and in that of one at the sixth month 6·67% albumen. Scherer, however, in that of one at the fifth month, found 7·67%, and only 0·82% in the fluid at the ordinary period of delivery.

In the physiological or normal condition no albumen is contained in the *excretions*, and its appearance indicates either disease of the excreting organ or a complete alteration in the composition of the blood.

The occurrence of albumen in the *urine* may be coincident with very different pathological conditions, although its presence was formerly made to constitute a special disease. Simon even asserts that he has often found albumen in the urine of persons, at all events, apparently healthy. In many acute and chronic diseases, unconnected with affections of the kidneys, albumen not unfrequently appears for a short time in the urine, as, for instance, in inflammations of the thoracic organs, acute articular rheumatism, intermittent fevers, typhus, measles, cholera, insufficiency of the valves or contraction of the orifices of the heart, also in chronic affections of the liver, and in pulmonary and peritoneal tuberculosis, especially towards the fatal termination of these diseases. The transitory passage of albumen into the urine appears to depend in these conditions on a change in the character of the blood, in consequence of which the albumen is able to penetrate through the tissue of the kidneys. It is, however, in affections of the kidneys, whether acute or chronic, that albumen appears most constantly in the urine. Bright's disease, is, as is well known, a term of very wide significance, but if we limit it as much as possible, and merely include under the term a degeneration of the tissue of the kidney, more especially of the cortical substance, whether of a fatty or other character, we may regard the presence of albumen in the urine as a constant symptom of this disease. But in transitory renal catarrh, such, for instance, as occurs in erysipelas nearly as frequently as after scarlatina, albumen, together with the well known epithelial cylinders of Bellini's ducts, is found as constantly in the urine as in inflammatory affections of the kidneys, where it is associated with the fibrinous plugs from the same ducts, and as in true Bright's disease. It is almost unnecessary to observe that the presence of pus or blood in the urine necessitates that of albumen, but it is worthy of notice that a little albumen, together with mucus-corpuscles is always found in uncomplicated severe catarrhs of the mucous membrane of the bladder.

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* Untersuch. üb. Eiter, Eiterung u. s. w. Erlangen. S. 75.

† Arch. gén. de Méd. 4 Sér .T. 19, p. 68.

‡ Heller's Arch. f. Chem. u. Mikrosk. Bd. 2, S. 218.

§ Zeitschr. f. wissenschaftl. Zool. Bd. 1, S. 88-92.

The observations already made in reference to the occurrence of albumen in the urine apply almost equally to its appearance in the *solid excrements*. Albumen is always found in the excrements in diarrhœa depending upon intestinal catarrh, and in diseases complicated with this affection; the quantity of the albumen increases, moreover, in proportion to the degree in which the blood becomes altered during the diarrhœa; hence, we find that not only in dysentery and cholera, in which so much stress has been laid on the discharge of albumen, but also sometimes in Bright's disease, albumen, together with entire patches of cylindrical epithelium, (in some cases the entire thimble-like coverings of the intestinal villi) is discharged in masses by the rectum.

Origin.—We have at present very little definite knowledge regarding the origin of albumen from the nitrogenous food. No doubt can be entertained that the chief source of the albumen of of the blood is to be sought in the protein-compounds contained in the food; for independently of the circumstance that direct experiments prove that animals cannot exist on food containing no protein-compounds, we find from comparative statistics of the food which has been taken, and of the nitrogenous matters expended in the metamorphosis of tissue, (See "Nutrition" in the third volume,) that the animal organism derives more than a sufficient supply of protein-compound from the ordinary vegetable food. Although we are not yet able to decide with absolute certainty on the incapability of the animal organism to generate albumen from other sources than protein-compounds, it yet appears highly probable that such is the case. We are not even acquainted with the mode of origin of the albumen of the blood from the allied protein-compounds contained in the food, as casein, vitellin, fibrin, legumin, &c.: all we know is that these bodies are converted by the process of digestion into substances differing very much in their physical properties from the above protein-compounds but resembling one another in their solubility in water, their insolubility in alcohol, and their incapability of coagulating. How and where these peptones become converted into the normal albumen of the blood, are points on which we are entirely ignorant, neither can we understand by what process the albumen acquires its due quantity of sulphur, since these peptones, as I have convinced myself, for the most part contain exactly as much sulphur as the substances from which they originate.

Uses.—After what has been said of the occurrence of albumen, it seems scarcely necessary to adduce any further proof of its utility in forming and renovating the nitrogenous tissues of the animal body. In fact the whole theory of nutrition rests on this postulate. It is a question that has been much contested and variously answered, whether albumen directly coöperates in the formation of cells and the elements of tissues. Jul. Vogel* is an especial supporter of the view that fibrinous exudations are alone adapted for the formation of cells and tissues; basing his opinion on pathologico-anatomical experiments on exudations, and on the fact that a small quantity of fibrin is contained in the lymph for the reproduction of effete materials. The absence of fibrin in the fluids of the egg, must also be considered as opposing Vogel's view, since these fluids exhibit the highest degree of plasticity; yet it must be admitted on the other hand, that this counter-proof is less worthy of attention from the circumstance that vitellin, which is the true germ of the egg, has been found by the most careful investigation to be more similar to fibrin than any other protein-compound, having, indeed, an almost perfectly identical composition with it. But independently of the peculiar relations of the germ of the egg, a careful consideration of plastic exudations will in itself lead us to doubt the correctness of Vogel's view, for how can the small quantity of fibrin in the plasma (see "Fibrin") give rise to the frequently large accumulations of fibrinous exudations that are passing into an organised condition, rapidly as the resorption of the serous portions of these exudations may be effected? We cannot suppose that Vogel intends to assert that it is only the fibrin of the exudations which is converted into cells and fibres. The following mode of considering the subject appears to correspond most closely with the facts before us. We shall in a subsequent part of the work enter upon the consideration of fibrin, as a link or transition stage in the metamorphosis of nitrogenous matters; we agree therefore so far with Vogel as to assume that all albumen passes through a transition stage, which we term fibrin, before it can be converted into cells and the elements of tissues: hence this intermediate link in the metamorphosis of tissue appears in very small quantity or not at all, because at this stage the metamorphosis is stationary for only a short time. If we regard fibrin as a body whose specific gravity is ever changing with its chemical changes, as, for instance, is the case with the aldehydes, it would scarcely remain for any appreciable length of time at a given stage of metamorphism, and would therefore be as little appreciable to our senses as the aldehyde of acetic acid, in the process of acid fermentation. We therefore believe that in the organisation of the exudations, fibrin is formed from the albumen of the transuded plasma, but that it rapidly undergoes further metamorphosis.

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* Path. Anat. S. 80 ff. [or p. 107, &c., of the English Translation. Vogel's opinion is not quite fairly stated in the text. His remarks apply solely to morbid *developments.*—G. E. D.]

It still remains, however, for us to determine why cells and fibres are not formed from serous exudations, that is to say, from albuminous solutions containing no fibrin. This question might perhaps be answered by supposing that the presence of fibrin is only required to form the point of crystallisation for the deposition of plastic matter, and this view seems to derive support from the fact, that a portion of coagulated fibrin when thrown into an uncoagulated plasma, perceptibly accelerates the coagulation of the fibrin; but so simple an explanation is probably not admissible, and it would rather seem that the serous exudations possess no tendency to become organised, in consequence of their never being pure plasma *minus* fibrin, but of their frequently containing less albumen, and in all cases more salts and extractive matters, than the serum of the blood; although we are unable to determine the manner in which salts are able to arrest the metamorphosis of albumen into cells, we yet know that other metamorphoses of albumen, as for instance, putrefaction, are hindered or modified by the agency of these bodies.

FIBRIN.

Chemical Relations.

Properties.—We must distinguish between numerous modifications of fibrin, if we would attempt to specify the various substances to which this term has been applied. We purpose, therefore, only to consider fibrin, in the first place, in its naturally dissolved form; next, in a spontaneous state of coagulation; and, lastly, when it is coagulated by heat, or boiled.

In the *natural solution of fibrin*, we can distinguish only a few of its properties, since it is here mixed with albumen and other matters of the serum of the blood; and we are acquainted with few reagents by which to distinguish dissolved fibrin in filtered frogs' blood (*i. e.* in blood deprived of its corpuscles), from the albumen contained with it in solution. We at present know nothing more of dissolved fibrin than the facts long ago advanced by Joh. Müller[*]. Neither acetic acid or caustic ammonia induces a precipitate in the fluid of frogs' blood; but a concentrated solution of caustic potash will precipitate fibrin as well as albumen (see p. 333); ether causes fibrin to coagulate, while it allows the albumen of frogs' blood to remain dissolved. The spontaneous coagulation of the fibrin from the plasma of all vertebrate animals may be greatly retarded by dilute solutions of the alkaline sulphates, nitrates, hydrochlorates, carbonates, and acetates, and may even be entirely prevented by concentrated solutions.

As we purpose treating somewhat fully of the spontaneous coagulation of fibrin in the second volume of this work, when we enter upon the consideration of the blood, we will now merely observe, that the *liquor sanguinis* (after the removal of the blood-corpuscles) will frequently assume a thick fluid and gelatinous character within two minutes after its removal from the living body; in a short time some drops of fluid appear on the tolerably consistent jelly, and speedily augment, until they form an entire stratum of serum over the now fully developed coagulum; this coagulum now begins to contract, becoming more or less tenacious, tough, elastic, and resistent, according to certain accompanying conditions (as we shall more fully explain when treating of the blood). If we trace this transition of the fibrin from the dissolved fluid condition into the solid state under the microscope, a careful observation shows us that the fresh *liquor sanguinis* exhibits nothing morphological beyond some few colourless blood-corpuscles; when it begins to gelatinise, separate points or molecular granules appear at various spots, from which arise extremely fine straight threads in radiating lines, although they do not form star-like masses as in crystallisation; these threads becoming elongated cross those springing from other solid points until the whole field of view appears as if it were covered with a delicate, but somewhat irregular cobweb. This net-work finally becomes so dense that the colourless blood-corpuscles imbedded in it can scarcely be distinguished.

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[*] Lehrb. d. Phys. Bd. 1, S. 117 [or vol. 1, p. 124 of the second Edition of the English Translation.]

It is scarcely necessary, at the present day, to offer any refutation of the older views, according to which, on the one hand, fibrin arose from the bursting of the colourless or even of the red blood-corpuscles, while, on the other, it was simply deposited from the blood in which it was originally only suspended. The former view has long ceased to be held by physiologists, while microscopic observations affords ample evidence of the untenability of the latter hypothesis.

As yet no satisfactory solution has been afforded to the question which has been frequently raised regarding the means by which the fibrin is held in solution in the circulating blood, and by which it is disposed to coagulate on the removal of the plasma from the living body. Various facts prove, indeed, that the access of the air (that is to say, of the oxygen,) greatly influences the coagulation of the fibrin; but it is doubtful whether this is the only cause of coagulation, since the same process goes on within the vessels of the living organism, as soon as the blood ceases to circulate. This question cannot be answered chemically, since we are at present acquainted only with the product of this process, while it is requisite for a correct judgment of it that we should know not only the end, but the beginning, that is to say, the substance originally held in solution in the blood. We must, therefore, still limit ourselves to the assertion that the blood of vertebrate animals holds a substance in solution, which, by its metamorphosis, generates a substance not soluble in the serum of the blood, and which we call fibrin.

The view that formerly prevailed, namely, that the fibrin was held in solution in the blood by alkalies and alkaline salts, and that its coagulation was owing to the decomposition of the combination of the fibrin and the alkali by the carbonic acid of the air, has been thoroughly refuted by Nasse*; indeed, blood containing much carbonic acid coagulates very slowly, and on the other hand, the carbonated alkalies retard, and may even wholly prevent the coagulation of the fibrin. If, therefore, we are determined upon seeking an explanation of this phenomenon, we must rest satisfied with mere fiction based upon analogy. Thus we may conceive that the albumen of the blood, while undergoing a process of metamorphosis, is disposed to assume a metamorphosed and insoluble form by the agency of the minutest quantity of oxygen, in the same manner as the juice of the grape, according to Gay Lussac's experiments, is brought into a condition of vinous fermentation by means of the minutest quantity of oxygen. But when so distinguished an enquirer as Nasse, while he declares this process to be a chemical one, regards the substance that undergoes the metamorphosis, as endowed with vitality, we are bound to reject his explanation as mere fiction; for, independently of the fact that if a process be chemical it must be capable of chemical explanation, it seems to us wholly at variance with all preconceived ideas of life to attribute life to a simple organic substance.

Spontaneously coagulated fibrin is a yellowish, opaque, fibrous mass, which becomes hard and brittle on drying; it is without smell or taste, and is insoluble in water, alcohol, and ether; after being dried it merely swells in water, and becomes again soft and flexible; it readily decomposes peroxide of hydrogen; it dissolves more easily in acetic acid and alkalies than many other protein-compounds; it decomposes rapidly and putrifies in the air, dissolving, if sufficient water be present, and becoming converted into a substance which, like albumen, is coagulable by heat; during this process it attracts a considerable quantity of oxygen, gradually developes ammonia, carbonic acid, butyric acid, and sulphuretted hydrogen, and leaves a residue consisting principally of leucine and tyrosine (Scherer,†

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* Handwörterb. d. Physiol. Bd. 1, S. 109 ff.

† Ann. d. Ch. u. Pharm. Bd. 40, S. 35.

Marchand,[*] Wurtz,[†] Bopp[‡]). It is generally supposed that spontaneously coagulated fibrin will dissolve in solutions of certain alkaline salts; but we should greatly err if we were to regard a fluid thus obtained as a simple solution; for fibrin not only requires a longer period to dissolve in a saline fluid than is necessary for the solution of a simple substance in an indifferent menstruum, but also a higher temperature, and the saline fluid must always be kept for one or more hours at a temperature approximating to the hatching heat (between 30° and 40°), before any considerable quantity of fibrin will be dissolved. Moreover, the fibrin should not be too long exposed to the action of the air, if we wish to effect its solution. Denis,[§] who first noticed this solubility of fibrin, Scherer,[||] and Polli,[¶] used for this purpose a solution of 3 parts of nitrate of potash in 50 parts of water. Zimmermann[**] has however shown that solutions of the alkaline sulphates, phosphates, carbonates, and acetates, as well as the chlorides, bromides and iodides, might be employed for the same object. The solution thus obtained, which is always imperfect, and contains undissolved portions requiring to be removed, is viscid, and at about 73° coagulates in flakes. It differs from an albuminous solution in being strongly precipitated by acetic acid (which is only the case to a slight degree with albumen when carefully neutralised); it is not coagulated by ether, in which respect it differs from the naturally dissolved substance which forms fibrin. When the fibrin has been digested for a sufficient length of time, the solution is not rendered turbid by dilution with water, as is the case after digestion for only a short period. At an ordinary temperature, the clear solution remains for a long time unaffected by the atmosphere, only depositing solid particles after it has absorbed oxygen, when it has passed into a state of putrefaction, and exhibits *vibriones*.

Scherer thought that he had proved that the fibrin from arterial blood or from venous blood in inflammatory diseases could not be converted into this albuminous substance by saline solutions. This view has been contradicted by Zimmermann, but the subject has not yet been fully investigated. My own experiments tend to show that the fibrin of the venous blood of the ox very speedily loses these properties, while that of the arterial blood of the same animal does not dissolve in a solution of nitrate of potash. In man I found that fibrin, whether from venous, arterial, or inflammatory blood, was soluble, excepting in two cases of inflammatory blood; the arterial and venous fibrin from pigs' blood dissolved equally well, and with great rapidity in water containing nitrate of potash.

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[*] Lehrb. d. physiol. Chem. S. 69.

[†] Ann. de Chim. et de Phys. T. 11, p. 258.

[‡] Ann. d. Ch. u. Pharm. Bd. 69, S. 16-37.

[§] Arch. gén. de Méd. 3 Sér. T. 1, p. 171.

[||] Op. cit.

[¶] Ann. univ. di med. 1839. Apr. pp. 25-33.

[**] Casper's Wochenschr. No. 30, 1843.

Boiled fibrin possesses almost all the properties common to coagulated albumen, from which it is extremely difficult to distinguish it. C. Schmidt[*] found the specific weight of dry fibrin extracted with water, alcohol, and ether to be =1·2678 after deducting the influence of the ash-constituents. The influence of heat deprives this fibrin of the property of decomposing peroxide of hydrogen, and of being converted into a soluble, albumen-like substance by digestion in solutions of alkaline salts. With acids and alkalies it reacts in the same manner as coagulated albumen; it dissolves in alkalies, and forms with them compounds having no reaction on vegetable colours; with acids it also forms combinations which are insoluble in water to which an acid has been added, but dissolve freely in pure water. Concentrated hydrochloric acid communicates an indigo-blue colour to it. By prolonged boiling in water, it becomes decomposed into a soluble and an insoluble compound, to the former of which Mulder[†] has given the name of teroxide, and to the latter, binoxide of protein. When decomposed by chromic acid, or by peroxide of manganese and sulphuric acid, it yields a larger quantity of butyric acid than any of the other protein-compounds or their derivatives; it yields, however, less acetic and benzoic acid than albumen, although more than gelatin (Guckelberger.[‡])

Composition.—Before we can consider the chemical constitution of a body, it is always necessary to inquire whether we have to deal with a pure and simple substance, with a chemical compound, or, as is often the case, with a body with which several substances are mixed. The question is more imperative in reference to fibrin than to any other animal substance, for both microscopico-mechanical investigations and many chemical experiments seem to indicate that the ordinary, so-called purified fibrin is not a chemically simple substance. Whether fibrin be separated from the blood or from the lymph, it is invariably found to be mixed with heterogeneous morphological elements, especially with the colourless blood-corpuscles, and what are termed the fibrin-discs, which are found associated with molecular granules of various kinds, and usually even with blood-pigment. A microscopic examination of coagulated and perfectly washed fibrin will readily prove that the mass under consideration is not of a homogeneous nature. It is a chemical fact that pure fibrin (even that of the pig, which dissolves so readily in a saline solution,) is incapable of complete solution, and always leaves a quantity of insoluble flakes. Even if Bouchardat's[*] statement is erroneous, as asserted by Dumas, Cahour,[†] and Mulder[‡], that he has decomposed fibrin into epidermose and albuminose, Mulder's experiments undoubtedly tend to show that more than one substance must lie concealed in fibrin; and this seems further proved by the above mentioned difference in the fibrin in different classes of animals, as well as by its different character in diseases, (the molecular fibrin of Zimmermann,[§] the parafibrin and bradyfibrin of Polli.[||]) Microscopical examination furnishes us, however, with the chief proof that fibrin is not a simple body.

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[*] Ann. d. Ch. u. Pharm. Bd. 61, S. 156-167.

[†] Ibid. Bd. 47, S. 300-328.

[‡] Op. cit.

In considering the elementary composition of this body, we must therefore always bear in mind that the results of the analyses refer to a mixed substance.

We will therefore content ourselves with giving the results of Scherer's and Mulder's analyses, in order to present some idea of the proportion of the various elements constituting fibrin.

	Scherer.	Mulder.
Carbon	53·571	52·7
Hydrogen	6·895	6·9
Nitrogen	15·720	15·4
Oxygen	22·814	23·5
Sulphur		1·2
Phosphorus		0·3
	100·000	100·0

Rüling[¶] found 1·319$\frac{0}{0}$ of sulphur in the fibrin of the blood of the ox, while Verdeil[¶] gave it as 1·593$\frac{0}{0}$. Most of the later elementary analyses of fibrin agree in the view that there is rather a larger quantity of oxygen contained in it than in albumen; Mulder therefore regards it as a higher stage of oxidation of his hypothetical protein, combined with sulphamide and phosphamide, and assigns to it the hypothetical formula, $(C_{36}H_{25}N_4O_{11}.2HO)+H_2NS+H_2NP$. Fats are always associated with fibrin; and although they have not been thoroughly investigated, they would appear to consist principally of soaps of ammonia and lime. (Berzelius[*], Virchow[†].) Dry fibrin contains about 2·6% of these fats.

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[*] Compt. rend. T. 14, p. 962.

[†] Ibid. p. 995.

[‡] Ann. d. Ch. u. Pharm. Bd. 47, S. 303-305.

[§] Zur Analysis und Synthesis der pseudoplast. Processe. Berlin. 1844. S. 110 ff.

[||] Gazeta med. di Milano, 1844, p. 118.

[¶] Ann. d. Ch. u. Pharm. Bd. 58, S. 312 u. 318.

Like all protein-compounds, fibrin contains mineral substances, of which the principal is phosphate of lime. Mulder found 1·7%, but Virchow only 0·66% of this salt mixed with a little carbonate of lime.

Compounds.—Fibrin-protein, binoxide of protein, corresponding, according to Mulder's hypothesis, to the formula $6(C_{36}H_{25}N_4O_{11}.2HO)+S_2O_3$, occurs, as we learn from the same observer,[‡] in most animal fluids, associated in larger or smaller quantity with fibrin. It may be obtained from boiled fibrin or vitellin, precisely in the same manner as albumen-protein from albumen, or by boiling the fibrin for a long time in water exposed to the air, or lastly by treating hair or horn with a solution of potash, filtering the boiled fluid, and precipitating with acetic or hydrochloric acid. It may be purified by repeatedly dissolving it in caustic potash, and precipitating it with acetic acid.

This body forms a light yellow, lumpy, tough precipitate, which, when dried in the air, cakes together into a blackish green, shining, resinous mass, and on trituration, forms a dark yellow powder; it becomes very viscid in warm water, and admits of being drawn into long, silky, shining bands and threads; it renders water in which it is boiled only slightly turbid, and is perfectly insoluble in alcohol and ether; in dissolves in dilute acetic acid and in dilute mineral acids; nitric acid does not communicate to it so well marked a yellow colour as to the other albuminous substances; when dissolved in acids it may be precipitated by yellow and red prussiate of potash, by tannic acid, and by acetate of lead; it is readily soluble in alkalies, from which it may again be precipitated by acids, it fuses on being heated, and finally carbonises, with the evolution of a horn-like odour.

Preparation.—The method first adopted by Joh. Müller is generally employed for obtaining the natural solution of the fibrin-yielding substance, viz., diluting frogs' blood with sugared water, (1 part of sugar to 200 of water,) and filtering it.

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[*] Lehrb. d. Chem. Bd. 9, S. 88.

[†] Zeitschr. f. rat. Med. Bd. 4, S. 269 ff.

[‡] Untersuch. übers. v. Völcker. H. 2, S. 253.

The best means of obtaining frogs' blood for this experiment is to amputate both thighs, and allow the blood, with which a considerable quantity of lymph is mixed, to flow into sugared water, which not only dilutes the *liquor sanguinis,* but retards the coagulation of the fibrin; the blood-corpuscles of the frog, like those of most of the other amphibia, are, as is well known, much larger than those of mammalia and birds, and therefore pass less easily through the filter.

A considerable quantity of the natural solution of fibrin may be obtained from human blood (the corpuscles of which have the property of sinking very rapidly), by pouring off the very slowly coagulating fluid which collects above the blood-corpuscles.

A single drop of fresh blood, when laid on the object stage and covered with a piece of glass, is sufficient to exhibit the coagulation of the fibrin under the microscope: on account of the mass of red corpuscles the coagulation is however not so well seen as when we employ a drop of fluid from the surface of blood, in which the red corpuscles have sunk below the upper level.

In preparing spontaneously coagulated and boiled fibrin, the blood-clot must be cut into fine pieces, and then washed in water until it appears perfectly white. The fibrin obtained in this manner is more readily washed than when obtained from whipped blood. The process of whipping consists either in shaking the blood, as it flows from the veins, in a bottle with shot, or rapidly stirring it with small twigs or rods; the blood-corpuscles remain suspended in the serum, while the fibrin separates in delicate but dense flakes; the greater density of the small *coagula* renders it difficult, however, to wash away the blood-corpuscles enclosed in these flakes, or to obtain the fibrin as free from hæmatin as that which is obtained from the blood-clot. In order to cleanse the fibrin as much as possible, it is necessary, first to knead it for some time in water, and then to hang it in water in a bag of linen, by which means the salts and the pigment gradually dissolve, and the particles of the fluid rendered thus heavier sink to the bottom of the vessel, while pure water rises in their place.

In order to obtain boiled fibrin in the greatest possible purity, we must dry it after it has been boiled in water; it should be then pulverised and extracted with alcohol containing sulphuric acid, in order to remove any remains of pigment, and finally with ether for the removal of the fat.

Tests.—It is only seldom that a case occurs in which any question can arise, as to whether the substance separated from an animal fluid is, or is not fibrin; thus, by way of illustration, the plasma surrounding the organs of insects coagulates on exposure to the air, and we may term this substance fibrin; yet it is by no means identical with the fibrin of vertebrate animals; for it does not separate under the microscope into threads, and it is insoluble in saline solutions, and even in solutions of the alkaline carbonates. Pathological fluids, on exposure to the air, occasionally deposit a sediment. But here the form of the coagulum as well as the microscopic texture of the sediment must decide whether or not the substance which is separated is fibrin; and the action of salts upon it may be observed in the further investigation. In many cases of this kind the separated substance is not fibrin, but consists of albuminous products, which appear under the microscope as minute masses or molecular granules, and whose chemical characters may be recognised by their behaviour with hydrochloric and nitric acids and other reagents; or finally it often consists of fatty or earthy matters that can easily be distinguished by the ordinary tests from true fibrin.

It is often perfectly impossible to distinguish coagulated fibrin from other protein-compounds; and we are therefore not justified in regarding every insoluble mass contained in an exudation as fibrin: the fibrin has, in these cases, already assumed an organised condition, and exhibits the elements of tissues under the microscope; or we find an unorganised, amorphous mass, which is usually not fibrin, although it may be a derivative of that body, and exhibits no property of fibrin that is not common to all the protein-compounds, as we see, for instance, in tubercular deposits. Many obvious reasons conspire to render a quantitative analysis impracticable in determinations of this kind. It is therefore unchemical, to say the least, for pathological anatomists to designate every unorganised exudation as fibrin; nor shall we learn to distinguish the chemical substrata of these exudations until we shall have thoroughly investigated, in a chemical point of view, the actual constitution of the protein-compounds.

The *quantitative determination of fibrin* in animal fluids has probably been more frequently attempted than that of any other substance; but we nevertheless are still without any method that fulfils the requirements of a good analysis. The usual method of determining fibrin quantitatively is by pressing the clot and washing out the blood, or more frequently by shaking or whipping blood before it has coagulated, and drying and then weighing the fibrin thus separated. In the former case, notwithstanding the most careful washing, the membranous cell-walls and the nuclei (if indeed they exist) of the red blood-corpuscles remain mixed with the coagulum; and there are also technical reasons why this method of treating the blood-clot should occasion a loss of fibrin; hence the second method is generally preferred. We have already seen that fibrin obtained by whipping always contains fragments of some of the red corpuscles and most of the colourless corpuscles; indeed the fibrin thus obtained is far more difficult to wash, and much less compact in its texture than that which is obtained from the blood-clot; it becomes somewhat reddish on exposure to the air, and often begins to putrefy before it has been freed from all soluble substances. The fibrin determined in quantitative analyses of blood and lymph is never or very rarely free from the fat which adheres most tenaciously to it. Moreover, in some forms of disease, and in certain animals, the blood when allowed to stand deposits a flocculent fibrin, which on washing passes to a greater or less degree through the filter.

If the separated fibrin were always of the same consistence, and if one and the same relation existed in every specimen of blood between the fibrin, the fats, and the colourless corpuscles, we might regard the analyses of different specimens of blood, in reference to the amount of fibrin, as always admitting of comparison; but we know that even under strict physiological relations, the quantity of the lymph-corpuscles suspended in the blood is extremely variable, and thus, for instance, we cannot strictly compare analyses of the blood after repeated venesections (when the blood always contains a very large number of colourless corpuscles) with those of blood not thus modified by venesection.

Physiological Relations.

Occurrence.—The substance which on coagulation forms fibrin occurs principally in the blood, in the lymph, and in the chyle.

Its amount in normal venous *blood* scarcely reaches 0.3%; according to most observers it fluctuates between 0·19 and 0·28%. In the blood of healthy men Scherer* found from 0·203 to 0·263%. This substance has, however, a higher importance than from its small amount we should at first suppose, seeing that, in different physiological and pathological conditions, its quantity is liable to greater variations than that of any other constituent of the blood.

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* Haeser's Arch. Bd. 10, S. 50.

Even *in different vessels* the blood contains different quantities of fibrin, although the question whether venous or arterial blood contain the greater quantity is still unanswered; at all events the blood of the portal vein contains a far less quantity of fibrin than that of the jugular veins; according to the numerous investigations of Schmid*, it is at least three times smaller in the former than in the latter. From some observations of Zimmermann,† it appears that the blood in the veins remote from the heart is richer in fibrin than that in the veins nearer to the central organ of circulation.

Sex appears to induce no difference in reference to the amount of fibrin in the blood, although the quantity of this constituent is affected both by the *period of life* and by *pregnancy*. According to the experiments of Nasse and the more recent investigations of Poggiale‡, the blood of new-born infants contains less fibrin than that of adults, the augmentation in the amount of fibrin being especially striking at the period of puberty. In pregnancy, as appears from the researches of Andral and Gavarret, it is principally in the last three months that the quantity of fibrin increases. During an *animal diet*, I found that my blood contained a larger amount of fibrin than during a *vegetable diet;* and Nasse§ has made experiments on dogs with a similar result. There are moreover many corroborative proofs of the correctness of Nasse's observation that the quantity of fibrin in the blood is increased during prolonged *fasting*.

The results independently obtained by Nasse‖ and Poggiale agree in showing that the blood of *herbivorous animals* generally contains more fibrin than that of the *carnivorous* (dogs and cats), and that the blood of *birds* contains even more than that of the *herbivora*.

The results of the quantitative determination of the fibrin in the blood in different forms of *disease* are very numerous, and on the whole tolerably accordant. The most constant and the most decided augmentation occurs in inflammatory diseases, and especially in acute articular rheumatism; in the last-named disease the fibrin has been found to reach 1·18$\frac{0}{0}$, and in pneumonia 1·01$\frac{0}{0}$.

It is moreover worthy of remark that inflammation in which no fever is present, and likewise mere fevers without inflammation augment the quantity of fibrin in the blood.

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* Heller's Arch. f. Chem. u. Mikrosk. Bd. 4, S. 97-132.

† Arch. f. phys. Heilk. Bd. 6, S. 586-600.

‡ Compt. rend. T. 25, p. 198-201.

§ Handwörterb. d. Physiol. Bd. 1, S. 148.

‖ Journ. f. pr. Ch. Bd. 28, S. 146 ff.

In other diseases, as for instance, in chlorosis, typhus, tuberculosis, Bright's disease, and carcinoma, there seems only to be an augmentation of the fibrin when an inflammatory complication supervenes; in carcinoma however, certain observations of Popp and Heller appear to indicate that there is a decided augmentation of the fibrin independently of any inflammatory fever.

There are no diseases in which we find a constant and certain diminution of the fibrin; and whenever we find any diminution of the fibrin it is always very slight.

It is however true that in diseases where a constant diminution of the fibrin has been supposed to exist, we have only rare opportunities of analysing the blood.

In the *lymph* of man Marchand and Colberg[*] found 0·052% and in that of the horse Geiger and Schlossberger[†] found 0·04% of fibrin.

In the *chyle* of a horse Simon found 0·075%, and in that of a cat Nasse found 0·13% of fibrin.

The fibrin in the *muscles* is by no means perfectly identical with spontaneously coagulated fibrin; it is one of the many species embraced under the generic name of fibrin.[‡]

We shall return to the consideration of the fibrin of the muscles (muscle-fibrin) when we treat of chemical histology; since, in order correctly to understand its relations, we must have an accurate knowledge of the histological elements of muscular tissue.

The remarks which have been already made on the manner of recognising fibrin, include all that need be stated in reference to the views advanced regarding the coagulated fibrin assumed to be deposited in tissues or exudations.

In the preceding description of fibrin, a criticism might probably have been expected on the several varieties of this substance, which have been described by different writers as occurring in morbid fluids; we have, however, made no reference to Nasse's fibrin-discs, to Zimmermann's molecular fibrin, to Rokitansky's pseudofibrin, or to the fibrin of later coagulation, to which Virchow attaches much importance, because we regard discussions on such points as out of place in the department of strict zoochemistry; for it is only after the principles of zoo-chemistry have been fully discussed, and when we enter on the theory of the animal [illegible], that we can form a sound judgment on such subjects.

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[*] Pogg. Ann. Bd. 43, S. 625-628.

[†] Arch. f. phys. Heilk. Bd. 5, S. 392-396.

[‡] [Liebig has recently published a memoir on the fibrin of muscular fibre, in which he indicates several points in which it distinctly differs from the fibrin of the blood. See Ann. d. Ch. u. Pharm. Bd. 73, S. 125.—G. E. D.]

Origin.—Taking into consideration everything connected with the occurrence of fibrin, we can scarcely entertain a doubt that it is formed from albumen, and not directly from the protein-containing food; for its occurrence in the chyle is not opposed to this view, partly because, as Henle has shown, fibrin may be conveyed in the fluid of the lymphatics and blood-vessels, and partly because, as I have fully convinced myself, all the juices of the animal body not only contain free carbonic acid but also free oxygen. It was formerly supposed that the formation of fibrin from albumen might very easily be accounted for, since, according to the older analyses of Mulder, fibrin contained one half less sulphur than the albumen of serum, nothing seemed more simple than to assume that the oxygen conveyed by the respiration to the blood, converted half of the sulphur of the albumen into sulphuric acid, and that this combined with an alkali, so that fibrin was now evolved. These and all similar views have become untenable since more recent analyses of albumen and fibrin have been made. If we would at present start an hypothesis regarding the formation of fibrin, it can only rest on the slight excess of oxygen which fibrin contains over albumen. The indication afforded by this fact has led, however, to serious error in reference to the increase of the fibrin in inflammations: since it was concluded that, although we may not know how the oxygen finds its way to the albumen to form fibrin, it is at all events incontestable that the latter is formed by a process of oxidation or eremacausis; and it was further very erroneously concluded that the augmentation of the fibrin in inflammation is dependent on an increased rapidity of the process of oxidation, and that consequently inflammation is nothing more than an actual process of *combustion*. This hypothesis originally propounded by chemists, was for a long period accepted by physicians, without any doubts occurring as to its correctness. In accordance with chemical principles, an excessive supply and absorption of oxygen *might* indeed be regarded as the cause of an increase of fibrin: but even this is by no means proved; for how would it then be possible that in pneumonia, where a greater or lesser part of the lungs is hepatised, that is to say, is rendered impermeable to air, a greater quantity of fibrin should be found in the blood than during other inflammatory affections? This has lately been referred to the greater frequency of the respirations, but independently of the circumstance, that in inflammation of other parts, the number of the fibrin should then attain at least the same height as in pneumonia, we know that fever, notwithstanding it is often accompanied by an increased frequency in the respirations, by no means gives rise to an augmentation of the fibrin. Physiological facts lead us to exactly the opposite hypothesis that *the augmentation of the fibrin in inflammatory blood is to be referred to a diminution in the supply of oxygen.* The frequent but short and incomplete respirations which occur only in febrile (and not in non-febrile) inflammations, are only sufficient to convey to the blood sufficient oxygen to convert certain substances into fibrin but not to oxidise them further; this is the reason why the amount of fibrin attains its *maximum* in pneumonia and pleuritis, and why the blood in the former disease is most rich in carbonic acid, for this gas is scantily excreted in proportion as oxygen is scantily received by the lungs. The physiological importance of fibrin affords arguments altogether in favour of this view.

Uses.—The phrases, *progressive* and *regressive* metamorphosis, of whose import we have spoken in an early part of this volume, (see p. 27,) have led to a long contest regarding the physiological importance of fibrin. On the one hand, it has been correctly maintained that this substance must be necessary to the formation of tissues, since as a general rule, the only exudations which are capable of organisation are those which contain fibrin; on the other hand, stress is laid upon the circumstance that an augmentation of the fibrin coincides with those states in which nutrition and renovation are most affected, and on the incontestable fact that the fibrin in the blood is found to be increased when more albuminous matters have been taken as food than could be applied to the reparation of effete tissue. We regard it, however, as superfluous to enter into the detailed arguments for and against these two opinions. The bearing of the whole case is simply this. It is pretty well established that fibrin is formed by a process of oxidation from albuminous matters; now we know that almost all the tissues are richer in oxygen than fibrin, and on the other hand, that the effete materials of tissue and the excess of nutrient matter can only be removed from the system, that is to say, be converted into ordinary excreta, by oxidation. Hence, the simplest view is to regard fibrin as representing a transition stage. If an albuminous body in the animal organism be more highly oxidised, it cannot altogether exceed the transition stage which is represented by fibrin, although indeed, the formation and increase of the latter may not always be evident. An analogous instance from pure chemistry will elucidate this view; we know, from Liebig's celebrated investigations on fermentation, the intermediate stages which during the process of acid fermentation present themselves between the two extremes of spirit of wine and acetic acid. We know that by a gradual process of oxidation, aldehyde and aldehydic acid are formed from the spirit, although these two substances may not become apparent: the beautiful investigation of Mulder regarding the *Mycoderma aceti* affords an almost more analogous illustration; its cellulose can only be produced by a process of oxidation from the alcohol; moreover, in the formation of this cellulose from the alcohol there must first be formed an aldehyde-like substance poorer in oxygen than cellulose; hence aldehyde may just as well be produced during the oxidation of alcohol into acetic acid, as during its oxidation into cellulose. In a perfectly analogous manner we may regard the fibrin as representing one of the stages in the oxidation of the albumen, which is transferred either into the tissues or into the secreted substances. There seems to us to be no discrepancy between the above observations on the chemical importance of fibrin, if we will only leave nature unfettered with divisions into progressive and regressive metamorphoses. For, if we assume the formation of tissue to be the highest stage of animal metamorphosis, fibrin pertains to the ascending or progressive series, inasmuch as it yields the proximate stratum for the development of cells and the formation of tissues; on the other hand, it must be classed in the descending or regressive series, in so far as its quantity in the blood is found to be increased in diseases, or after the excessive use of albuminous food, when it does not become converted into tissue but is changed by oxidation into the ordinary excreted matters. For we cannot believe that, as in the percussion-apparatus of Physicists, a given quantity of fibrin will repel and displace a corresponding amount of tissue. In short, we seem to be nearest the truth in regarding fibrin as representing one of the most common stages in the metamorphosis of albuminous substances.

We must not conclude our observations on fibrin without noticing a very common error that has crept into pharmacology from the misunderstanding of a chemical fact. Many physicians believe that the antiphlogistic power of nitrate of potash is explained by the chemical fact that spontaneously coagulated fibrin dissolves in a solution of nitre. Without entering into the question whether this salt actually possesses the power ascribed to it, we assert that this mode of explanation is altogether untenable, for it is difficult to draw the conclusion that nitre can prevent the formation or augmentation of fibrin in inflammatory blood, simply because coagulated fibrin is soluble in a solution of this salt. According to Scherer, the fibrin of inflammatory blood appears to be insoluble in this saline solution; how then can a solution of nitre prevent the augmentation of fibrin in inflammatory blood through a solvent power which, in relation to this inflammatory fibrin, it actually does not possess?

There would be much more probability in the assumption that a solution of nitre hindered the coagulation of highly fibrinous blood, or that it redissolved already coagulated fibrin. The most simple arithmetical example will illustrate this view. Scherer asserts that 1 part of nitre is required to dissolve 1·5 parts of fibrin; assuming that the quantity of the blood amounts to twenty pounds, and that it contains only 0·3% of fibrin, the whole amount of fibrin would be not less than 300 grains, and to dissolve this quantity 200 grains of nitre should be at once taken; physicians, however, usually prescribe about 10 grains every two hours, so that in 24 hours 100 or 120 grains are at most all that is taken to act upon the fibrin. But the amount of nitre in the blood can never rise even to this insufficient height, partly because the salt becomes distributed from the blood-vessels into the juices of the body generally; and partly because it is much too rapidly carried off by the urine to admit of its accumulating in great quantity in the blood. Even if it were possible to prove that nitre possesses this power, it would be very singular and inexplicable why we never class amongst the special antiphlogistic medicines other salts, as, for instance, the alkaline carbonates, which possess a much greater power of dissolving fibrin, and of preventing its coagulation.

In this pharmacological digression, we cannot help remarking that if inflammation were actually a process of oxidation or combustion, it is very strange that we have not found the alkaline salts of the vegetable acids, the amylacea, and the fats, to be the most efficient antiphlogistics. It is true that we attack severe inflammation with tartar emetic, but even when given according to Rasori's method, it communicates to the blood so little combustible material as to be inappreciable, especially when combined with an antiphlogistic diet. If inflammation were a process of combustion, the antiphlogistic diet must be exactly the reverse of that which we understand by the term. Moreover, direct experiments on patients, to whom large doses of acetate and tartrate of potash might safely be administered, have proved that these salts exert no action either of a beneficial or of an injurious character, on the inflammatory process. Even the most zealous adherents of the chemico-pathological theory of combustion would hardly attempt to regard the fat in the emulsion as an antiphlogistic, since it has been already proved by Nasse and others that the fibrin of inflammatory blood, and of the *crusta inflammatoria*, contains nearly twice as much fat as ordinary fibrin, unless, indeed, he would attempt to trace to this fact the *digitus index medicatricis naturæ*, protecting the fibrin from the action of the oxygen through the agency of combustible fat.

VITELLIN.

Chemical Relations.

Properties.—This is the albuminous body of the yolk of egg; it is so similar to albumen that, until recently, it has been confounded with the albumen of the white of egg; like the latter, it exists both in a *soluble* and in an *insoluble modification;* the former is not precipitated from its aqueous solution by organic acids or by ordinary phosphoric acid, but is thrown down by sulphuric and hydrochloric acids; at 60° its solution begins to become opalescent, and at from 73° to 76° there is a deposition of larger or smaller flakes. It is only distinguished from soluble albumen by the circumstances that (without the addition of acetic acid or of salts) when heated, it forms flakes and clots, that it is not precipitated by the salts of oxide of lead or of copper, and that it is thrown down by ether.

Coagulated vitellin has the same properties as coagulated albumen, and the similar modifications of the other protein-compounds. Moreover, in its reactions it coincides with Mulder's binoxide of protein or fibrin-protein.

Composition.—Dumas was the first who analysed this body, and discovered that it differed from albumen; according to this analysis, with which that subsequently made by Gobley* very well agrees, vitellin contains 3 atoms of water more than albumen; according to Gobley it also contains phosphorus and sulphur. Mulder, and especially v. Baumhauer†, have subsequently made accurate analyses of this body, and regard it as a combination of oxide of protein with sulphamide, so that its theoretical formula would somewhat resemble that of fibrin. According to v. Baumhauer, the phosphorus contained in vitellin exists in it solely in the form of phosphate of lime; moreover his amount of sulphur is obviously too small, since he only determines this substance in the moist way.

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* Journ. de Pharm. T. 11, pp. 410-17, et T. 12, pp. 5-12.

† Scheik. Onderzoek. D. 3, p. 272, or Arch. der Pharm. Bd. 45, S. 193-220, and rs. *H.* 2, S. 80.

To give a general idea of the composition[*] of this body, we append the mean numbers obtained by Gobley and by v. Baumhauer.

	Gobley	v. Baumhauer.
Carbon	52·264	52·72
Hydrogen	7·249	7·09
Nitrogen	15·061	15·47
Sulphur	1·170	0·42
Phosphorus	1·020	—
Oxygen	23·236	24·30
	100·000	100·00

Berzelius conjectures that we are here not dealing with a simple substance, but with an admixture of substances, as is unfortunately the case with most of the protein-compounds. Vitellin, extracted with indifferent menstrua, contains 4·043% of phosphate of lime.

Preparation.—*Soluble* vitellin, in a pure state, that is to say, free from yolk-fat and from yolk-globules, has not yet been exhibited. Gobley has only attempted to ascertain its reactions after stirring the yolk of egg with water and allowing the emulsive constituents, as much as possible, to deposit themselves. In its *coagulated* form we can obtain it in a far purer state; boiled and triturated yolk of egg is extracted with ether, alcohol, and water, then dissolved in acetic acid, and precipitated therefrom by ammonia, with, however, such precaution that the fluid remains sufficiently acid to retain the phosphate of lime in solution; the gelatinous precipitate is then dried and extracted with water and alcohol.

Tests.—The methods of recognising and quantitatively determining vitellin are sufficiently obvious from our description of the properties of this body.

Physiological Relations.

Occurrence.—Hitherto vitellin has only been recognised in the yolk of egg, of which, according to Berzelius[†], it constitutes about 17%, or, according to the most recent investigations of Gobley,

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[*] [Vitellin has also been recently analysed by Noad. See the Chemical Gazette, vol. 5, p. 409. G. E. D.]

[†] Jahrb. d. Ch. Bd. 9, S. 650.

15·76%. No eggs but those of the common hen have as yet been examined.*

Origin.—It is very easy to conceive that vitellin may be formed from albumen or fibrin, but in the yet imperfect state of our knowledge regarding albumen and fibrin as well as vitellin, we cannot chemically trace out this metamorphosis. Since, however, it is poorer in carbon, and somewhat richer in oxygen, than albumen, it may, like fibrin, be regarded as one of the first stages of the metamorphosis of albumen by the action of oxygen, and as a certain form of non-spontaneously coagulating fibrin.

Uses.—From the position in which vitellin occurs and from its analogy with other albuminous substances, it is obviously one of those nutrient substances which are employed in the formation of the animal tissues. We are however entirely ignorant of the chemical equations representing these changes; from the admirable work of Baudrimont and Martin St. Ange† we may however at least draw the conclusion that this substance loses a portion of its nitrogen and assimilates oxygen in its conversion into tissue. (See the "History of Development" in the third volume.)

GLOBULIN.

Chemical Relations.

Properties.—This body, which has also received the name of *crystallin,* occurs naturally in the soluble state, but becomes insoluble on boiling. *Soluble* globulin, when dried at 50°, forms a yellowish, transparent mass, which may be easily triturated, and then yields a snow-white powder; it is devoid of smell and taste, swells like albumen in water, and gradually dissolves, forming a viscid solution containing merely a few flakes; after precipitation by alcohol from this solution, it is insoluble in water, but, like casein, is partially soluble in boiling alcohol; on cooling, however, it again separates from this solution. The aqueous solution of globulin is coagulated by ether. When dried, the soluble modification may be heated to 100° without passing into the insoluble state. It is distinguished from albumen and vitellin, which are very similar to it, by the following properties; its solution does not become opalescent at a lower temperature than 73°; at 83° it assumes a milky turbidity, and at 93° separates as a globular mass (if it be still mixed with hæmatin) or as a milky coagulum which never becomes clear on filtration, and from which neither small quantities of acetic acid or ammonia separate flakes capable of being removed by filtration; it is only when neutral alkaline salts are added, and the solution is then boiled, that the fluid becomes perfectly clear and flakes and small clots are deposited. The following reaction is very characteristic of globulin; its solution is not precipitated either by acetic acid or by ammonia, but it becomes strongly turbid when the fluid treated with acetic acid is neutralised with ammonia, or conversely when after the addition of ammonia it is neutralised with acetic acid. Its behaviour simply with acetic acid is, however, also different from that of albumen. On the addition of a little dilute acetic acid, the solution of globulin becomes opalescent, and when heated to 50° a milky coagulum separates; the fluid rendered turbid by a little acetic acid, becomes clearer when more of the acid is added, but always remains opalescent; this fluid does not coagulate till heated to 98°; it is only when a very great excess of acetic acid has been added that the globulin ceases to be coagulable by heat. The behaviour of globulin towards mineral acids and metallic salts is precisely the same as that of albumen. It is also coagulated by creosote; it decomposes and becomes putrid much more readily than the other protein-compounds; when boiled it developes ammonia.

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* [Gobley has recently examined the eggs of the carp, which in their chemical composition seem very similar to those of the common hen. Journ. de Chim. méd. T. 6, p. 67.—G. E. D.]

† Ann. de Chim. et de Phys. T. 21, pp. 195-257.

Lecanu regarded this body as identical with albumen, Simon with casein; we would rather place it by the side of vitellin, if the elementary analyses were not opposed to this view; but it appears to us by no means advantageous to science, to group together several ill-defined substances merely on the strength of a few reactions, and without any definite proof of their similarity.

Berzelius ascribes to the globulin, united in the blood with hæmatin, the singular property of dissolving in water containing albumen and little or no salts, but not in water which holds in solution large quantities of alkaline salts. He was in error in regarding the sediment of the blood-corpuscles which he named hæmatoglobulin, as a simple mixture of globulin and hæmatin; for we shall shew, in the second volume (in the section on "the blood"), that this hæmatoglobulin is composed of blood-corpuscles which by the law of endosmosis become so distended in pure water as scarcely to be visible under the microscope, but which (unless the blood-corpuscles have burst from too great an addition of water) again become apparent when we add a salt to the fluid in which they are immersed, and thus render it denser; in which case the blood-corpuscles again contract, become denser and flatter, and are again visible.

No properties have yet been detected in coagulated globulin by which it may be distinguished from other boiled protein-compounds.

Composition.—Globulin has been subjected to even fewer analyses than vitellin; as that which is contained in the blood can never be perfectly freed from hæmatin, no accurate analysis can be made of it. Dumas* has however analysed a specimen containing hæmatin, while both Mulder† and Rüling have analysed this substance as obtained from the crystalline lens.

	Mulder.	Rüling.
Carbon	54·5	54·2
Hydrogen	6.9	7·1
Nitrogen	16·5	37·5
Oxygen Sulphur	22·1	
		1·2
	100·0	100·0

Although Berzelius assumed that phosphorus as well as sulphur was contained in this substance, Mulder found only the latter, which averaged 0·265%: this sulphur was however determined in the moist way; in the dry way, I determine the sulphur in globulin from the crystalline lens of the calf (as a mean of three experiments) at 1·134%, and Rüling‡ in globulin similarly obtained from the ox at 1·227%. Mulder, at present, regards globulin as a combination of his hypothetical protein with sulphamide.

The globulin of the crystalline lens contains only a very small amount of insoluble ash-constituents; I found only 0·241% of phosphate of lime.

In globulin from the crystalline lens of a calf I found 1·548% of soluble salts consisting of metallic chlorides, sulphate of soda (=30·37% of the soluble salts) and alkaline phosphates (=7·77% of the soluble salts), but containing no alkaline carbonates. On the other hand, on evaporating the fluid filtered from the coagulated globulin (which besides 92·095% of coagulated globulin yielded 7·905% of soluble residue) I obtained on the incineration of this residue an ash which contained only 13·166% of phosphate of lime, while the soluble salts contained a large quantity of alkaline carbonates, namely 16·71%.

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* Compt. rend. T. 22, p. 904.

† Journ. f. pr. Ch. Bd. 19, S. 189; and Bullet. d. Néerl. 1839, p. 196.

‡ Ann. d. Ch. u. Pharm. Bd. 58, S. 313.

Now as the ash of non-coagulated globulin contains no alkaline carbonate, we may conclude that in soluble globulin soda is combined with an organic substance—either with the globulin itself or with an organic acid,—and that after the destruction of the globulin this free alkali combines with the sulphuric acid produced from the globulin, which would account for the circumstance that the ash of the collective globulin contains no alkaline carbonate; if, on the other hand, the soluble salts are separated from the globulin on its coagulation (in the same manner as albumen on coagulation loses its alkali) they contain much alkaline carbonate after the combustion of the organic substance not separated with the coagulated globulin, for here there is no formation of sulphuric acid to decompose the alkaline carbonates. No alkali occurring in the ash as a carbonate, can, according to my view, be combined with the globulin previously to its coagulation, for the following reason. The solution of globulin from the crystalline lens has a distinct, although a very faint *alkaline* reaction; during the process of coagulation we may easily show that it developes ammonia, and afterwards the fluid does not, as in the case of albumen, exhibit a stronger alkaline reaction, but on the other hand is now *acid;* this phenomenon cannot be more simply explained than by the assumption that there is *phosphate of soda and ammonia* in the fluid, for the solution of this salt has an alkaline reaction, loses ammonia on boiling, and finally assumes an acid reaction when the salt is thus converted into acid phosphate of soda. Now if globulin were contained in this fluid, no acid reaction could ensue after its coagulation, because the soda separated from the globulin would take the place of the ammonia that escaped from the phosphate. Hence this soda which is combined with carbonic acid in the ash of the residue from which all globulin has been removed, must have been previously in combination with an organic acid. If for the present we regard this organic acid as lactic acid, until the subject can be more accurately investigated, we can scarcely be charged with adopting too bold an hypothesis, since this acid cannot at all events be one of the volatile acids of the animal body. We are unfortunately still compelled to rest upon such deductions as these in our endeavour to investigate the nature of the salts held in solution in association with animal substances, since as we shall subsequently see (when treating of "the mineral constituents of the animal body,") the constituents of the ash unfortunately afford very little information regarding the actual constitution of the salts that existed previously to the calcination of the residue. I must moreover remark, that the boiling must be continued for some time, in order that the acid reaction after the coagulation of the globulin may manifest itself.

Preparation.—As in the case of soluble albumen, it is impossible to prepare *soluble globulin* in a perfectly pure state. Globulin presenting the reactions which we have already indicated, may be obtained by neutralising with acetic acid the fluid of the crystalline lens, evaporating it to dryness at a temperature not exceeding 50°, and extracting the residue with ether and dilute alcohol. The globulin of the blood, which cannot be separated without decomposition of the hæmatin, presents, with the exception of its colour, exactly the same relations as the globulin obtained in the above manner from the crystalline lens.

Mulder prepared *coagulated globulin* by simply extracting with alcohol and ether globulin which had been precipitated by boiling. The coagulated globulin which I examined was precipitated with hydrochloric acid, washed with the same acid, then dissolved in water, again precipitated by carbonate of ammonia, and finally washed with water, alcohol, and ether, after which it left no perceptible ash.

Tests.—In the preceding remarks we have mentioned the reactions by which globulin may be distinguished from the similar protein-compounds: we will here merely add that no other *soluble* protein-compound is precipitated both from its acid and its alkaline solution by neutralisation, although almost all the insoluble protein-compounds possess this property—a circumstance which affords a proof that globulin is reduced to the coagulated state both by an excess of alkali and by an excess of acid. In our observations on casein, we shall point out how it may always be distinguished from that substance. It will always be difficult—indeed at present it is impossible—to recognise globulin with certainty when it is mixed with albumen or casein. Here, unfortunately, elementary analysis affords us no assistance, since it so closely approximates in its ultimate constitution to other protein-compounds.

In attempting a *quantitative determination* of globulin we must adopt the same precautionary measures as in the determination of albumen; indeed, as we have already shown, there are even greater difficulties in reducing globulin to a condition in which it can be easily and thoroughly collected on a filter, than are presented by albumen. We must acidify with acetic acid and apply heat ; then saturate the acid with ammonia, and boil strongly and for a considerable time, in order to obtain the globulin in a state admitting of its being readily collected on a filter. Even if we succeeded in distinguishing globulin from any similar body, as for instance, albumen, by its relation to acetic acid, and by noticing its behaviour when heated to 50° (see p. 370,) or by observing that it was precipitated by the neutralisation either of its acid or its alkaline solution, we could not by these means separate it from that body; for it would not be in a state fit for filtration, that is to say, it would either pass through the filter in a turbid condition, or it would stop up the pores of the filter and could not by any possibility be washed off.

Physiological Relations.

Occurrence.—Globulin occurs in the cells of the *crystalline lens* in a very concentrated solution. In the human lens Berzelius* found 35·9% of dry globulin.

Globulin is one of the principal constituents of the *blood*, since, with hæmatin, it forms the viscid fluid contents of the blood-corpuscles.

We can form no definite and certain idea regarding the quantity of globulin contained in the blood-corpuscles, for even if we are able to form an approximative idea of the amount of hæmatin contained in the corpuscles (see p. 305) we have no means of deciding how much of the remainder of them (amounting to 94·28%) is to be ascribed to fat, to the enveloping membrane, and to globulin. Hence it is not possible to make any accurate statement regarding the quantity of globulin contained in the blood generally. We shall, however, return to this subject in the second volume, when treating of "the blood-corpuscles."

Globulin has not yet been found in any other parts of the animal body. In the present state of organico-analytical chemistry we are unable to attempt to seek it in its coagulated state.

Origin.—In regard to the seat of the formation of globulin, no reasonable doubt can be entertained that it at present has only been found in cells and cell-like bodies like the blood-corpuscles.

Whichever view we adopt regarding the mechanical mode of formation of the red from the colourless corpuscles (see p. 306) and the remarks "on the blood-corpuscles," in the second volume) we must arrive at the conclusion, that the globuloid is formed within a cell or a vesicle or a closed saccule, which is bathed in an albuminous fluid. If albumen lies without the enveloping membrane and globulin exists within it, we are almost compelled to assume that the globulin is produced by the cellular action from the albumen, but we cannot give the chemical equation, representing how this transformation takes place, for the simple reason that we are ignorant of the rational composition both of albumen and globulin. From a comparison of the analyses of albumen and globulin, we can, however, perceive that the latter contains a little less carbon and sulphur, but rather more oxygen than the former. (Little weight can be attached to the amount of phosphorus in albumen, in consequence of the uncertainty connected with our modes of determining that element.) Hence globulin appears to be albumen modified by oxidation, so that it is allied to fibrin, or perhaps more correctly should be placed between this substance and albumen. Moreover, the physiological hypothesis, according to which the blood-corpuscles are to be regarded as nothing more than laboratories in which the ordinary nutrient matter, crude albumen, is first prepared, in order to become applicable to the formation or reparation of tissues in different organs, corresponds with this view. Whether globulin be directly converted into fibrin, is a question which at present is unanswerable; we shall, however, return to this subject in a future part of this work.

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* Lehrb. d. Ch. Bd. 9, S. 528.

Uses.—The object of nature in depositing globulin in the cellular fibres of the crystalline lens is too obvious to require comment. It is, however, interesting to observe that nature, in producing a refractive fluid, aimed at rendering the lens achromatic, not merely by anatomical structure, but also by filling its middle layers with a concentrated fluid which is always attenuated toward the capsule.

Chenevix is the first to whom we are indebted for this observation; he found that the specific gravity of a lens weighing 30 grains, taken from the eye of the ox, was 1·0765, while, when he had peeled off the outer layers, the nucleus, weighing 6 grains, had a specific gravity of 1·194.

But how nature, to carry out this object, effects the separation or secretion of pure globulin, free from albumen and hæmatin, in the crystalline lens, from the minute capsular artery, will probably never be understood.

From the above observations it is manifest that we can never understand the importance and the uses of the globulin in the blood until we have obtained an accurate knowledge both of its chemical constitution, and of the function of the blood-corpuscles.

CASEIN.

Chemical Relations.

Properties.—In its dry state *soluble casein* occurs as an amber-yellow mass, devoid of odour, insipid and viscous when tasted, and having neither an acid nor an alkaline reaction; it dissolves in *water*, forming a yellowish viscid fluid, which on evaporation becomes covered with a white film of insoluble casein which may be readily drawn off. If a concentrated solution of casein be exposed for a long time to the air, it rapidly passes into a state of *putrefaction*, developing a very large quantity of ammonia, and yielding leucine, tyrosine, and similar substances.

Alcohol renders casein opaque, and gives it the appearance of coagulated albumen; a part, however, of the casein dissolves in alcohol, and on evaporation can be again obtained in an unchanged state; in boiling alcohol it dissolves more freely, but on cooling, the greater part of the casein again separates; this casein thus treated with alcohol dissolves tolerably readily in water, especially with the aid of heat, and has all the properties of non-coagulated casein. If we add a little alcohol to a concentrated aqueous solution of casein, a precipitate is thrown down which, however, dissolves again readily in water; if, however, the precipitation be effected by the free addition of strong alcohol, the casein is then difficult of solution or even insoluble in water. By *boiling* it is not coagulated from its solutions.

Acids precipitate casein from its aqueous solution, and partially combine with it, but they do not reduce it to the coagulated state, for on neutralisation with alkalies or metallic oxides, the casein again dissolves; these combinations of casein with acids are readily soluble both in pure water and in alcohol. Casein is especially distinguished from albumen by the circumstances that it is precipitated from its aqueous solutions by *acetic* and *lactic acids*, the precipitate not being an acetate or a lactate, but pure casein. The precipitate is only slightly soluble in an excess of acetic acid; like all the other combinations of this class with acids, it is precipitated by ferrocyanide of potassium. The alcoholic solution of casein is not only not precipitated by acids, but alcohol even possesses the property of dissolving those combinations of casein with acids, which are insoluble in water. When treated with concentrated *nitric, hydrochloric,* or *sulphuric acid*, casein yields the same products of decomposition as albumen and fibrin. *Tannic acid* precipitates it from very dilute aqueous and alcoholic solutions.

Casein combines very readily with *bases*, turbid solutions of this substance becoming clear on the addition of caustic *alkalies; alkaline earths* dissolve in solutions of casein, and can only with difficulty be separated from that body; with larger quantities of these earths casein forms insoluble compounds. Hence its solutions are precipitated by chloride of calcium and sulphate of lime, as well as by sulphate of magnesia, *on the application of heat*, which thus afford a reaction very characteristic of casein. It resembles albumen in being precipitated by *metallic salts*, and forming with them two combinations, namely, one of casein and the acid, and the other of casein and the metallic oxide. Ferrocyanide of potassium does not throw down casein from alkaline solutions, and only induces a slight turbidity in neutral solutions.

These are the properties of casein, as it occurs in its ordinary state of solution in the milk; if, however, we obtain it perfectly free from alkali, according to Rochleder's* method, which we shall presently give, it presents some characters different from those which we have just described. For instance, it dissolves only very slightly in pure water, rather better in hot water, and not at all in alcohol; it reddens blue litmus without, however, communicating this property to water, but it forms solutions with carbonate and phosphate of soda, which no longer exhibit an alkaline reaction; it dissolves very readily in solutions of hydrochlorate of ammonia, nitrate of potash, and other neutral alkaline salts, does not coagulate on boiling, like albumen, but forms on evaporation a film of casein as we have already described. It dissolves in dilute mineral acids, but is precipitated on the addition of an excess of the acid; the solutions of casein in dilute acids become covered on evaporation with this colourless, transparent, and somewhat tough membrane; the solution of this substance in acids or in alkalies is completely precipitated by neutralisation, and mineral acids throw it down from its acetic acid solution. The precipitated hydrochlorate of casein is, like the hydrochlorate of albumen, soluble in pure water; before dissolving, however, it swells, like the latter, into a jelly-like mass; both acids and alkalies precipitate it from this solution; the deposit thrown down by hydrochloric acid swells and finally dissolves in alcohol, but is precipitable from this fluid by ether, this precipitate being again soluble in water. The mere boiling of a solution of casein, under no circumstances, induces a precipitation. On the other hand, we may be readily led to believe that it is converted into a coagulable substance when we have dissolved it in a solution of carbonate of potash, or of nitre to which a little potash has been added; on neutralising this solution with an acid, a transitory precipitate ensues on stirring or shaking the mixture, and if we now boil the fluid, there is formed an abundant thick coagulum; I have not been able to persuade myself to regard this as a modification of casein coagulable by mere heat (such as sometimes appears to be contained in the milk) but I rather incline to the belief that the acid has converted only a part of the caseate of soda occurring in solution, and of the simple carbonate of soda, into acid salts, and that on the application of heat it is only the acid salts remaining in solution which are decomposed and evolve carbonic acid, while the casein is precipitated.

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* Ann. d. Ch. u. Pharm. Bd. 45, S. 253.

From the above observations it follows that casein is not reduced to its *coagulated* state by the same means as albumen and globulin. We have long been acquainted with the fact that the casein in milk is coagulated by the mucous membrane of the stomach of the calf; our knowledge is, however, by no means clear regarding the peculiar condition under which this coagulation ensues. We have seen that soluble casein, on the evaporation of its solution, is partially transformed into the insoluble modification; cases, however, occur, in which the whole of the casein in milk is rendered insoluble by evaporation. Even on prolonged exposure to the air, it is well known that milk coagulates; the casein thus separated reacts in the same manner as the precipitate obtained from a solution of pure casein by means of lactic acid, that is to say, after treating it with carbonate of lime or baryta, it is only slightly soluble in water, most of it having been transformed into the insoluble modification. Simon* and Liebig explain the coagulation of casein by the calf's stomach (rennet) by assuming that the latter primarily acts as a ferment, converting the sugar in the milk into lactic acid, which precipitates the casein; Simon moreover maintains that he has observed that solutions of casein free from milk-sugar are not coagulated by rennet. Certain experiments, instituted by Selmi†, are, however, opposed to this view; he found that alkaline milk could be coagulated by rennet in the course of ten minutes, and that, after the coagulation, it still had a decidedly alkaline reaction; the same was observed when milk, artificially rendered alkaline by the addition of soda, was exposed to the action of rennet. Conversely, casein dissolved in an excess of acetic or oxalic acid, coagulated, like the alkaline solution, at a temperature of from 50° to 56°. The true cause of coagulation is still entirely unknown. It appears, however, from the observations of Scherer*, that casein cannot coagulate in the form of a membrane, unless in the presence of oxygen.

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* Frauenmilch. S. 29.

† Journ. de Pharm. T. 9, pp. 265-267.

From the large number of individual facts which we have mentioned in relation to casein, it may be inferred that our knowledge of this substance is still very defective; for otherwise we could have embraced in a few paragraphs the most essential points in relation to this body; our difficulties are increased by the probability that casein is not to be regarded as a simple organic body, but as a mixture of at least two different substances. Mulder† and Schlossberger‡ have especially directed attention to this circumstance. If freshly washed casein be digested for a couple of days with dilute hydrochloric acid, it is found to be perfectly dissolved; by neutralisation with carbonate of ammonia there is precipitated from this fluid a white, viscid body, difficult to separate by filtration; but in the neutralised fluid there still remains in solution another substance which may be thrown down by an excess of hydrochloric acid; and the hydrochloric acid even now holds in solution a protein-like body. The first of these bodies was found by Schlossberger to contain sulphur, and the second to be free from that element.

Here, however, it might be supposed that the prolonged digestion of the original casein with the dilute hydrochloric acid had decomposed it into several substances. Another and an earlier experiment of Mulder, however, supports the view that casein consists of several substances. To milk which had been as thoroughly as possible freed from butter-globules by chloride of sodium, Mulder added dilute hydrochloric acid, which yielded the ordinary precipitate; there remained, however, in solution, a similar body, which was not precipitated till this mixture was boiled.

It is very difficult to arrive at a definite opinion on this point; for any one repeating the experiments on casein which have been described by different authors, will find that all the statements regarding this substance confirm one another to a certain degree, but that on often repeating the same experiment differences present themselves which thus explain the discrepancies in the statements of different observers. Casein appears to us to be a highly transmutable substance, often undergoing change on the application of the mildest reagents. In a word, a method of preparing casein, which would exclude all suspicion of its being changed by the process, is still a desideratum. The circumstance that the elementary analyses of the separated matters give such slightly different results, adds very much to our difficulty of ascertaining whether the constitution of casein is simple or complicated.

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* Ann. d. Ch. u. Pharm. Bd. 40, S. 36.

† Berzelius Jahresbr. Bd. 26, S. 910.

‡ Ann. d. Ch. u. Pharm. Bd. 58, S. 92-95.

Casein, when thoroughly *coagulated* by rennet, and purified, is hard, and presents a yellowish translucent appearance; it softens and swells in water, but is insoluble both in that fluid and in alcohol. Like its soluble modification it combines with *acids* and *alkalies*; but on separating the inorganic part from the casein, the latter is insoluble in water. In its relation to the stronger mineral acids it in every respect resembles coagulated albumen; it is as difficult of solution in acetic acid as its soluble modification; alkalies dissolve it very readily, and, if concentrated, decompose it like the other protein-compounds on the application of heat. On *heating* casein, it softens, may be drawn out in threads, and becomes elastic; and at a higher temperature it fuses, swells up, carbonises, and developes the same products of distillation as albumen and fibrin; when strongly heated in the air it burns with a flame, and, unless carefully washed with acidulated water, leaves an ash containing carbonate and phosphate of lime, but no alkali.

The investigations of Iljenko* show that casein during its putrefaction, (even when perfectly freed from fat) developes at first carbonate of ammonia and hydrosulphate of ammonia, but that, after a space of from two to five months, its principal products are ammonia, valerianic acid, butyric acid, and leucine, and to these substances Bopp† adds a white, crystallisable, sublimable body, having a very strong fæcal odour, and an acid which, when decomposed with a mineral acid, yields a brown substance together with tyrosine, and ammonia. On fusing casein with hydrated potash, it developes a very large quantity of hydrogen and ammonia, leaving much valerianic acid in combination with the potash, and likewise leucine and tyrosine. (Liebig.‡) When decomposed with chromic acid, or with sulphuric acid and binoxide of manganese, casein yields much more acetic acid, oil of bitter almonds, and benzoic acid, but much less valerianic acid and butyric acid than fibrin; in reference to the quantities of these products of decomposition it most nearly resembles albumen, although it yields a larger amount of acetic acid. (Guckelberger.[*])

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* Ann. d. Ch. u. Pharm. Bd. 55, S. 78-95, and Bd. 58, S. 264-273.

† Handwörterb. der Chemie v. Liebig, Wöhler u. Pogg. Bd. 3, S. 220.

‡ Ann. d. Ch. u. Pharm. Bd. 57, S. 127-129.

Simon has directed attention to certain differences presented by casein from *women's milk*, cows' milk, and the milk of the bitch. Casein from women's milk is white or yellowish, friable, becomes moist on exposure to the air, is insoluble in alcohol, but dissolves in water, forming a turbid, frothy fluid, from which it is completely thrown down by tannic acid, acetate of lead, and corrosive sublimate, and imperfectly precipitated by acetic acid and alum. Casein from *cows' milk* is not so freely soluble in water, and, when dry, is tough and horny; while that from the *milk of the bitch* is not tough and horny, and is difficult of solution in water. Dumas has, however, ascertained that the composition of these three kinds of casein is perfectly identical. There is much here that requires explanation. Simon's observations are certainly correct; and can not only confirm his statements from my own experience, but also those of Elsässer, according to which the cheesy coagulum of women's milk is always loose and jelly-like in its texture, while that of cows' milk is very firm and clotty. These differences may, however, be found to depend on many external relations, on the admixture of various substances, &c. Thus, for instance, I believe that the jelly-like coagula of women's milk are more dependent on the alkaline state of the fluid than on any peculiarity in the casein; at all events, I have found that women's milk, when acid, yields a much thicker coagulum than when alkaline, and cows' milk, when alkaline, a much looser coagulum than when acid;—facts of the highest interest and value in relation to dietetics.

Composition.—Casein, like albumen, has very often been analysed, but all these analyses have led to no perfectly certain empirical formula, and far less to a rational one. We give as examples, analyses by

	Mulder.[†]	Scherer.[‡]	and Dumas.[§]
Carbon	53·83	54·665	53·7
Hydrogen	7·15	7·465	7·2
Nitrogen	15·65	15·724	16·6
Oxygen Sulphur	23·37	22·146	22·5
	100·00	100·000	100·0

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[*] Ann. d. Ch. u. Pharm. Bd. 64, S. 39-100.

[†] Bullet. de Néerl. 1839, p. 10.

[‡] Ann. d. Ch. u. Pharm. Bd. 40, S. 40.

[§] Compt. rend. T. 21, p. 715.

According to more recent investigations purified casein contains 0·85% of sulphur.

In casein, precipitated by acetic acid, and washed with alcohol and ether, Rüling[*] found 1·015% of sulphur; but in casein which had been precipitated by acetic acid, dissolved in carbonate of soda, and again precipitated by the acid, the quantity was only 0·850%; Walther[†] found 0·933%, and Verdeil[‡] 0·842% of sulphur in casein, which had been treated with hydrochloric acid and carbonate of soda.

According to Mulder, casein is nothing more than his hypothetical protein combined with sulphamide. No formula for casein can, however, be established till the question is definitively settled whether it be a simple or a compound body.

Casein that has not been treated with acids contains about 6% of phosphate of lime; more, consequently, than is contained in any of the protein-compounds we have hitherto considered.

Preparation.—We obtain soluble casein by evaporating skimmed milk, extracting the residue with ether, and dissolving it in water; we then throw down the casein from the aqueous solution by the addition of alcohol, with which we must also carefully wash the precipitate.

Berzelius precipitates the casein from skimmed milk by sulphuric acid, rinses the white coagulum with water, and decomposes the sulphate of casein with carbonate of lime, or (which is better) with carbonate of lead; the casein which is dissolved in water always contains a little lead, which, however, may be removed from the solution by sulphuretted hydrogen.

Simon removed the fat, by means of alcohol and ether, from casein precipitated by sulphuric acid, before decomposing it with carbonate of lime.

Mulder prepared casein for elementary analysis by precipitating it from skimmed milk, by warming it with acetic acid, washing and thoroughly rinsing the precipitate with water, separating the fat by boiling alcohol, and finally, by drying at 130°.

According to Rochleder's[§] method skimmed milk is coagulated with dilute sulphuric acid, (acetic acid or hydrochloric acid may however be used in its place;) the precipitate is then duly pressed and again dissolved in a dilute solution of carbonate of soda; this solution is allowed to stand for some time in a shallow vessel, when there gradually forms on its surface a layer of fatty matter, which we must remove as completely as possible with a spoon, or else we must decant the subjacent fluid with a syphon. The fluid is now again precipitated with an acid, and the previous steps are repeated. After the casein has been thrice dissolved in carbonate of soda, and the fat as often skimmed off, the last trace of fatty matter may then be easily removed by alcohol and ether, which otherwise is a very difficult task. Casein thus prepared may moreover be rendered entirely free from acid by repeated boiling in water; so that if, for instance, it has been precipitated with sulphuric acid, chloride of barium does not excite the slightest turbidity when added to its acid solution. Bopp* adopts a modification of Rochleder's method; he precipitates a solution of casein in carbonate of soda with hydrochloric acid, and repeatedly washes this precipitate with water containing 2% or 3% of hydrochloric acid; it is then mixed with pure water, in which it swells and gradually dissolves, especially if the temperature be raised to about 40°; the solution contains hydrochlorate of casein, from which the casein must be thrown down by careful neutralisation with an alkali, and the precipitate then washed.

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[*] Ann. d. Ch. u. Pharm. Bd. 38, S. 309.

[†] Ibid. Bd. 37, S. 316.

[‡] Ibid. Bd. 38, S. 319.

[§] Ibid. Bd. 45, S. 253-256.

Tests.—It is now ascertained that no reliance is to be placed on certain properties of casein which were formerly regarded as characteristic indications of its presence, and it is unfortunately the case that recent investigations have only shown us the fallacy of our former tests, without affording us better and more certain means of detecting it. There were three especial properties by which it was generally believed that casein might be recognised. In the first place the capability of an animal fluid *to form a membrane* on evaporation, was regarded as the most certain sign of the presence of casein; we have however already shown (p. 334) that both alkaline albuminates and acid solutions of albumen equally possess this property, and, indeed, that the fluid filtered from ordinary coagulated albumen always contains such an albuminate, and consequently has a tendency to form such a membrane; the tendency of an albuminous fluid to form a membrane on evaporation, is directly proportional to the amount of alkali or albuminate which it contains, and it is this circumstance that has led some very accurate observers to believe that they have found casein in the blood and in fluid exudations, where in reality not a trace of this substance occurs.

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* Ann. d. Ch. u. Pharm. Bd. 69, S. 16-37.

[Since the publication of this volume in German, two memoirs on the assumed discovery of casein in the blood have appeared, one by Guillot and Leblanc,* the other by Panum.† G. E. D.]

This error would be further promoted by a second mode of testing for casein, namely, by its property of being *precipitated by acetic acid;* this was regarded as a means of distinguishing between casein and albumen; but if the slight turbidity which affects albuminous solutions (see p. 333), when they are neutralised or very much diluted with water, occasionally gave rise to a confusion between these substances, this must have occurred far more frequently when it was believed that the albumen had been removed by boiling from albuminous fluids; for there then remains, as we have already seen, a little coagulated albumen with soda or potash in solution; by the addition of acetic acid the albumen is precipitated from this solution in precisely the same manner as casein, which is not the case with the unboiled albuminate of potash. Every accurate experimenter must have thus been led (till these facts were ascertained) to believe that he had always found a little casein in the fluid filtered from coagulated albumen.

The third means of discovering casein is the only one now left us; and even this, by its incorrect application, has already given rise to false conclusions. We refer to the *coagulability of casein by rennet*,—a test by which some have supposed that they have detected casein in the blood: but in order that the casein may be separated by this means, the rennet must be tolerably fresh, or at all events must not have become putrid, when it is placed in the fluid which is to be examined; the mixture should then digest, at a temperature of 40°, for a period not exceeding two hours; if no coagulum is then formed, we are not justified in assuming that casein exists in the fluid; for if we allow the rennet to remain for twenty-four hours or longer in the fluid at that temperature, putrefaction ensues, with the development of *vibriones*, and the fluid becomes turbid by the products of putrefaction, but not by coagulated casein. Blood in which, for instance, some chemists fancy that they have thus detected casein, putrefies, on the addition of rennet, after a considerable time, but I have never succeeded in obtaining from it a true coagulum of casein.

Sulphate of magnesia and *chloride of calcium* have been recently recommended as very good tests for the presence of casein; the casein separating *on boiling* in combination with magnesia or lime; but unfortunately albuminate of soda (which, as we know, does not coagulate on boiling) possesses this property in common with casein.

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* Compt. rend. T. 31, p. 585.

† Arch. f. pathol. Anat. Bd. 3, S 251.

At an earlier period of organic chemistry, many other reactions by which casein was characterised used to be described, as, for instance, sulphurous acid, its difficult solubility in acetic acid, &c.; but all these means yield no definite result. Moreover, during the last few years, much attention has been devoted to the behaviour of casein and of the protein-compounds generally with tests of the most varied kind; but however deserving of notice such endeavours may be, they have not produced any great results, nor indeed could they be expected to do so, for independently of the fact that an endeavour to discover any decisive reactions is mere groping in the dark, when the investigation is not guided by one uniform leading idea, the results of these experiments so frequently vary in their individual character that it is often impossible to bring them into harmony. Any one who has occupied himself with such investigations, and observed the action of acids, bases, metallic salts, &c., under various relations, on the albuminous substances, can confirm the statement that one and the same substance, under apparently similar relations, yields the greatest diversity of reactions, sometimes presenting a similarity to one and sometimes to another protein-compound. The various relations which modify these reactions, and of whose nature we are still ignorant, render experiments perfectly useless, unless these circumstances be taken into account. In general we may suspect the modifying influence, but in special cases we are often quite in the dark. A very simple example will illustrate our meaning. Casein is sometimes very readily soluble in acetic acid, at other times it is rather difficult of solution, while again there are other occasions in which it is almost insoluble in that fluid; we can only conjecture that the state of cohesion, the earthy matters contained in it, &c., give rise to this difference; but in individual cases it is often impossible to say which of these two conditions, or whether any other, is influencing the result of the special observation.

I may in this place give another example of the difference induced by inexplicable circumstances on reactions: on one occasion a turbid acid solution of casein becomes perfectly clear on the application of heat, on another the casein is entirely separated on heating; and thus acetic acid not unfrequently produces only a slight precipitation in the milk of cows and other animals, a true coagulum only separating on boiling.

In order to determine with any certainty whether casein exists in an albuminous fluid, we should conduct our experiment in the following manner. The fluid must be boiled for some time, a little hydrochlorate of ammonia having been first added, to effect the separation of the albuminate of soda; we must then filter it, and ascertain whether sulphate of magnesia or chloride of calcium yields a precipitate without the aid of heat; if such a precipitate be formed, we remove it by filtration, before boiling the fluid, in order to search for casein. If a precipitate be formed on boiling the fluid thus prepared, the presence of casein must in this case be shown by rennet.

Acetic acid was formerly almost the only reagent employed in the *quantitative determination* of casein; but this acid by no means effects a thorough precipitation of the casein, and when added in excess it often dissolves a very considerable portion;—an observation which formerly led Schübler to the belief that the milk contained a peculiar substance, to which he gave a special name, *zieger*.* The best method of analysing milk which has yet been proposed is, unquestionably, that of Haidlen.† On stirring milk with about one-fifth of its weight of finely pulverised gypsum, and heating it to 100°, a perfect coagulation ensues, and we obtain on evaporation a brittle, easily pulverisable residue, from which ether and alcohol easily remove the fat, milk-sugar, and most of the salts. The residue is then not pure casein, but the quantity of that ingredient in a state of purity may be easily calculated by determining the quantity of fat, sugar, and salts contained in the milk.

Physiological Relations.

Occurrence.—Casein occurs, as is well known, in the milk of all the mammalia.

Clemm‡ found 3·37%, and Fr. Simon,§ on an average, 3·5%, of casein in *women's milk;* the latter found 4% in the colostrum, but only 2·15% in the milk six days after delivery. In women's milk of good quality Haidlen‖ found 3·1%, but in milk of an inferior character only 2·7%.

In *cows' milk* Boussingault¶ found the casein to range from 3%

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* [Zieger is, literally, a sort of whey.—G. E. D.]

† Ann. d. Ch. u. Pharm. Bd. 45, S. 273 ff.

‡ Inquis. chem. etc. Götting. 1845.

§ Frauenmilch. Berl. 1838.

‖ Ann. d. Ch. u. Pharm. Bd. 45, S. 273 ff.

¶ Ann. de Chim. et de Phys. 3 Sér. T. 8, p. 98.

to 3·4%, Playfair determined the average at 4·16%, Poggiale[*] at 3·8%, and Simon at 7%.

In the *milk of bitches* Simon found 14·6% of casein, Dumas[†] from 9·73% to 13·6%, and Bensch[‡] from 8·34% to 10·24% (including the insoluble salts.) In asses' milk Peligot[§] found 1·95% and Stiptr. Luiscius and Bondt[‖] 2·3%; the latter found 16·2% in mares' milk; in goats' milk, Payen found 4.52%, Stiptr. Luiscius and Bondt 9·12%, and Clemm 6·03%; Schlossberger[**] found 9·66% in the milk of a he-goat, and Stiptr. Luiscius and Bondt 15·3% in ewes' milk

According to Dumas and Bensch the milk contains more casein during an *animal* than during a strictly vegetable diet.

The nitrogenous substance to which we apply the name of casein, occurs in the milk, for the most part, in a state of solution, but a not inconsiderable portion forms the free investing membrane or wall of the milk-globules. The microscope alone affords us no information regarding the structure of this membrane; hence we do not attach much faith to the assertions of Raspail and Donné,[††] who were the first to assume the existence of such a membrane: Simon[‡‡] believed that he had detected fragments of these membranes in milk which had been evaporated and treated with ether; Henle[§§] was the first to demonstrate its existence; on examining under the microscope the gradual action of acetic acid on the milk-globules, he noticed a decided distortion of this membrane. The best proof of the existence of an investing membrane is, however, afforded by an experiment instituted by E. Mitscherlich: on shaking perfectly *fresh* milk with ether, it is scarcely at all changed, the ether merely taking up a little fat; now, if the milk were a simple emulsion, it would yield all its fat to the ether, and would be converted into a transparent, tolerably clear fluid; as this is not the case, the separate fat-vesicles must be surrounded by an insoluble substance; if now we add a substance capable of dissolving these membranes, ether when shaken with milk will act on it precisely as on an emulsion, that is to say, it will take up the fatty matter;

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[*] Compt. rend. T. 18, pp. 506-507.

[†] Ibid. Bd. 21, S. 708-717.

[‡] Ann. d. Ch. u. Pharm. Bd. 61, S. 221-227.

[§] Ann. de Chim. et de Phys. T. 62, p. 432.

[‖] Mémoires de la Soc. de Méd. de Paris. 1787, p. 525.

[**] Ann. d. Ch. u. Pharm. Bd. 51, S. 431.

[††] Cours de Microscopie, p. 356.

[‡‡] Medic. Chem. Bd. 2, S. 75, or English Translation, vol. 2, p. 43.

Fror. Notiz. 1839, Nr. 223, and Allgemeine Anatomie, S. 942.

and indeed this is the case if a little caustic or carbonated alkali be added to the milk before it is shaken with ether. Mitscherlich, by this beautiful experiment, has removed all doubt regarding the existence of such a membrane. I have, however, observed the following facts: on placing under the microscope milk shaken with ether but to which no potash has been added, the surface of the milk-globules appears of diminished transparency, opaque, and fissured; in short, the wall presents the appearance of being coagulated. In place of potash I have used phosphate of soda and sulphate of soda; milk, treated with the former, yielded almost all its fat to ether, but did not become so clear as when treated with potash; under the microscope the aqueous fluid exhibited only a few fat-globules, which were *no longer round* but corrugated, of a caudate form, &c. Sulphate of soda has the property of causing the capsules of the milk-globules to burst, after which the fat can be extracted from the milk by ether; the watery fluid, however, remains very turbid, but no longer exhibits under the microscope either milk-globules, or shreds of destroyed capsules, but only extremely minute, scarcely isolable, molecular granules, which are unquestionably the fragments of the destroyed capsules, and do not consist of finely comminated fat; for, on the addition of a little potash, they not only do not disappear under the microscope, but the fluid which had previously retained its milky colour becomes perfectly clear and limpid. Hence we perceive that our ordinary casein not only contains the protein-compound dissolved in the milk, but likewise another, which forms the capsule of the milk-corpuscles, so that we thus also have a microscopico-mechanical proof of the composite nature of ordinary casein.

It was formerly supposed that casein existed in other animal fluids and solid parts, and indeed it was regarded as a normal constituent of the blood. In our consideration of the means by which casein may be recognised with certainty, we have, however, shown that no reliance can be placed on statements of this nature. Hence we can attach no weight to the assertions that casein occurs in the urine or in effusions within the peritoneum, the pleura, or the arachnoid, and the cases where, in consequence of metastasis of the milk, casein actually occurs in the urine or other fluids, require no further mention. The same remark holds good in reference to the supposed occurrence of casein in the saliva, in pus, tubercles, and other morbid products.

Origin.—In our entire ignorance of the true chemical constitution of casein, we cannot resort to any experiment to elucidate its mode of formation. Although we are unable distinctly to recognise the presence of casein in the blood, there is no doubt that it is formed there, and that it is merely separated by the mammary glands. We must clearly understand the differences in the constitution of albumen and casein before we can venture to offer a conjecture regarding the conversion of one into the other.

Uses.—The occurrence of casein in the milk, the best of all kinds of food, leaves no doubt regarding the uses of this substance: especially since we see how nature provides that more casein is always supplied for the building up of the bodies of very young animals, than is required for their future support. Casein not only yields to the infant body the material by which soft parts are nourished and caused to grow, but likewise conveys into the system a sufficient quantity of bone-earth and lime to cause the skeleton of the infant body gradually to attain its necessary solidity.

We now proceed to notice the chemical relations of certain substances which, perhaps, strictly speaking, do not belong to animal chemistry, since they occur only in the vegetable world: but there are two reasons, a chemical and physiological reason, why they should be noticed in the present place. In a chemical point of view they deserve notice, because we thus become acquainted with new protein-compounds, very similar to those already described, but yet differing from them, and thus obtain a more perfect insight into the whole group of this class of bodies; and in a physiological point of view they are of at least equal importance, for it is from them that the animal protein-compounds, which we have already described, are formed in the organisms of herbivorous animals, and that the solid substrata of the body are deposited in the various tissues. The actual physiological importance of these substances will be noticed when we enter upon the subject of "Nutrition."

GLUTEN.

Properties.—This substance, to which the name *phytocolla* has also been applied, is, when dried, transparent, very hard and difficult to pulverise; when moist it is adhesive, viscid, and elastic; it is insoluble in cold, and very slightly soluble in hot water; it dissolves readily in boiling alcohol, from which water again precipitates it; it is also precipitated from its alcoholic solution by corrosive sublimate and acetate of lead; it dissolves imperfectly in acetic acid, and hence does not seem to be a perfectly pure protein-compound. In other respects it has all the properties of the protein-compounds.

Composition.—Gluten from several sources has been submitted to analysis; but here, as in the case of all the protein-compounds, no satisfactory formula has been calculated.

The following are the results of some of the analyses of this body:

	Scherer.[*]	Jones.[†]	Heldt.[‡]	Mulder.[§]
Carbon	54·6	55·22	56·26	54·84
Hydrogen	7·4	7·42	7·97	7·05
Nitrogen	15·8	15·98	15·83	15·71
Oxygen	22·2	21·38	19·94	21·80
Sulphur				0·60
	100·0	100·00	100·00	100·00

The sulphur in gluten has been accurately determined by Rüling[||] and Verdeil;[¶] the former found 1·134% in wheat-gluten and the latter 0·985% in rye-gluten.

It is obvious that the numbers yielded by the above analyses differ too widely to admit of our attempting to calculate a trustworthy formula.

Preparation.—As this body especially occurs in the seeds of the cereals, the best method of obtaining it is by sufficiently kneading their flour under water, boiling the residue with alcohol in order to effect a perfect removal of the starch, and filtering while hot; on cooling and evaporating the solution, it is precipitated in white flocculi.

LEGUMIN.

Properties.—This body forms either a white, nacreous, iridescent precipitate, or else is thrown down in a flocculent form; when dry, it has a yellow, transparent appearance, and is brittle. It coagulates like albumen from its aqueous solution, but is precipitated from it by acetic and phosphoric acid like casein, from which, however, it differs, in the first place, in not dissolving in concentrated acetic acid, and, secondly, in the circumstance that when it is precipitated by an acid, the precipitate does not dissolve when digested with carbonate of lime or of baryta. It is coagulated by rennet. It dissolves readily in ammonia and other alkalies.

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[*] Ann. d. Ch. u. Pharm. Bd. 40, S. 7.

[†] Ibid. S. 65-70.

[‡] Ibid. Bd. 45, S. 191.

[§] Versuch einer allg. phys. Ch. 1844. S. 308.

[||] Ann. d. Ch. u. Pharm. Bd. 58, S. 310.

[¶] Ibid. S. 318.

Composition.—No definite results have as yet been obtained from the analyses of legumin. The following numbers have been found by the chemists whose names are attached to each analysis:

	Dumas & Cahours.[*]	Jones.[†]	Rochleder.[‡]	Rüling.[§]
Carbon	50·50	55·05	56·24	50·59
Hydrogen	6·78	7·59	7·97	6·83
Nitrogen	18·17	15·89	15·83	16·54
Oxygen Sulphur	24·55	21·47	19·96	25·57 0·47
	100·00	100·00	100·00	100·00

The differences presented by these analyses are so great that it is obvious that we have not yet succeeded in obtaining this substance in a state of purity, and fit for elementary analysis.

Preparation.—This body is chiefly found in peas and beans, and other leguminous seeds, from which it may be easily obtained; the watery extract of these seeds has an acid reaction, and on neutralisation the legumin is precipitated; it is purified by solution in ammonia, from which it is again precipitated by an acid, and finally by extraction with alcohol and ether.

Besides these substances, there are in the vegetable kingdom, and especially in seeds, other substances which approximate more or less closely to the protein-compounds of the animal kingdom. In the first place there is *vegetable albumen*, which Liebig calls *vegetable fibrin;* it is insoluble in water, and similar in its composition to coagulated animal albumen; it remains undissolved, when we have separated the starch from flour by washing, and the gluten by alcohol. Of the *diastase* or *mucin* which is formed during the germination of grain, and which is a product of the metamorphosis of the previous substances, we know even less, both in reference to its composition and its properties. It appears from the investigations of Ortloff* and Buckland W. Bull† that the *emulsin* or *synaptase* obtained from almonds is not a protein-compound; indeed this is sufficiently obvious from the large quantity of oxygen (26·56$\frac{0}{0}$) which it contains.

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[*] Ann. de Chim. et de Phys. T. 6, p. 409.

[†] Ann. d. Ch. u. Pharm. Bd. 40, S. 67.

[‡] Ibid. Bd. 46, S. 155.

[§] Ibid. Bd. 58, S. 301-315.

There are several animal substances pertaining to the protein-compounds of which we have no more accurate knowledge than we have of the above named vegetable substances; in this category we may place *keratin*, the substance deposited in horny tissue, (which, according to Mulder, is the same oxide of protein as exists in fibrin, but combined with a far larger quantity of sulphamide,) the substance termed *mucin*, peculiar to mucus, and the *pyin*, existing in pus and morbid tumours, of which full notice will be taken when we treat of the chemical theory of the tissues and juices. In the same manner we shall treat of *pepsin* and the *peptones* when we enter into the special consideration of the digestive process.

TEROXIDE OF PROTEIN (PROTEINTRITOXYD.)

Chemical Relations.

Properties.—When dried, this substance is brittle, and easily pulverisable, but when moist it is tough, viscid, capable of being drawn out in threads, and when warmed has an odour resembling that of gelatin; it is soluble in water, but insoluble in alcohol and ether, and in the fatty and volatile oils; it has no reaction on vegetable colours. It is precipitated from its solution by dilute mineral acids, chlorine water, tannic acid, corrosive sublimate, the salts of the oxides of lead, silver, zinc, and iron, but not by ferrocyanide of potassium, the alkaline salts, or chloride of barium. With alkalies it forms neutral compounds, from which it is also precipitated by metallic salts. When boiled with caustic alkalies it developes ammonia, and becomes converted into a substance, which, according to Mulder, is the true teroxide of his protein, in accordance with his latest formula, $C_{36}H_{25}N_4O_{10}+3O+3HO$.

Composition.—This body was discovered and analysed by

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* Arch. d. Pharm: Bd. 48, S. 12-27.

† Ann. d. Ch. u. Pharm. Bd. 69, S. 145-162.

Mulder*; from the mean of five analyses it was found to contain:

Carbon	51·69
Hydrogen	6·64
Nitrogen	15·09
Oxygen	26·58
	100·00

In his most recent memoir Mulder regards this substance as a combination of true teroxide of protein with ammonia, in accordance with the formula $H_4NO + 2\ (C_{36}H_{25}N_4O_{13}) + 3HO$.

Preparation.—Mulder originally obtained this substance by treating his albumen-protein with chlorine, whereby he obtained the body which he then termed chlorite of protein; this substance when decomposed with ammonia yielded the body in question.

He subsequently ascertained that he could obtain it by the prolonged boiling of fibrin or albumen in water, if freely exposed to the air; the solution which is thus obtained is filtered and evaporated, and the residue extracted with alcohol; the portion insoluble in alcohol is again dissolved in water and precipitated by basic acetate of lead; the precipitate after being thoroughly washed is then decomposed by sulphuretted hydrogen, the sulphide of lead removed by filtration, and the solution evaporated.

Tests. This body has so few characteristic properties, that in the present state of our knowledge it is extremely difficult, if not impossible, to distinguish it with perfect certainty from those substances which frequently occur, although only in small quantities, which have been hitherto named extractive matters soluble in water.

The peptones, ptyalin, pyin, and other little investigated animal matters are very similar to this substance, but differ from it in some of their characters, and hence must not be regarded as identical with it, although many of the differences may be dependent on the admixture of other matters with them. Hence organic analytical chemistry has here a great blank to fill up in order to elucidate the actual conditions under which this substance occurs. Unfortunately it cannot be obtained in a state of purity from the animal fluids, so that we cannot have recourse to an elementary analysis to confirm our diagnosis.

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* Journ. f. pr. Ch. Bd. 22, S. 340; Bull. de Néerlande, 1839, p. 404; Ann. d. Ch. u. Pharm. Bd. 47, S. 300-320.

Physiological Relations.

According to Mulder this body exists in normal blood and in all fluid exudations, and hence also in pus; and its quantity is very considerably increased in the blood in inflammatory diseases. He regards the *pyin* discovered by Güterbock in pus as altogether identical with this substance; but if for the reasons we have already given in reference to testing for teroxide of protein, we cannot regard it as positively decided that this substance occurs in all these animal fluids, yet it is probable from the mode in which it is artificially prepared, that a substance which is formed from albumen or fibrin in warm water exposed to the air, also occurs in the blood where the above named substances which yield it, are exposed to similar influences. If more accurate investigations confirm the existence of this teroxide of protein in the manner that Mulder supposes, we shall then acquire a knowledge of an important intermediate link in the metamorphoses of the animal tissues, and in particular we shall have considerably approximated to the yet unsolved problem of the conversion of albuminous bodies into bodies yielding gelatin, or of fibrin into tissue.

DERIVATIVES OF THE PROTEIN-COMPOUNDS.

The bodies of this group present very great differences in their physical and chemical properties; except that they all contain nitrogen, and that they occur only in the animal body, where they form the chief groundwork of the tissues, there is scarcely a point of general resemblance between them; in their behaviour towards acetic acid and ferrocyanide of potassium, and towards concentrated hydrochloric and nitric acids they exhibit none of the essential characters of the protein-compounds. Only four of these substances have as yet been accurately studied, although regarding even their intimate chemical constitution there is as much doubt as in the case of the protein-compounds.

ANIMAL GELATIN.

Under the term gelatin we comprehend those animal substances which do not exist ready formed in that state in the animal organism, but are produced from certain animal parts by mere boiling with water, so that the still undescribed substance from which this body is so easily obtained, may be regarded as the organic substratum of most of the animal fluids. All these very similar bodies, to which we give the common name of *gelatin*, are especially distinguished by the following properties; they swell and become very translucent in cold water; they dissolve in hot water; on cooling they separate as translucent, lubricous masses, and are precipitated from the most dilute solutions by chlorine, tannic acid, and most of the salts of the earths and metals.

There are two principal varities of gelatin to be considered, namely, *bone-gelatin*, *carpenter's glue*, or *glutin*, and *cartilage-gelatin* or *chondrin*, although here, as in the case of protein, there appear to be several modifications of each variety.

GLUTIN.

Chemical Relations.

Properties.—In a state of purity, glutin appears in colourless, transparent pieces, which are hard, horny, brittle, heavier than water, devoid of taste and smell, and exhibit no reaction on vegetable colours; on trituration it does not adhere to the pestle like the protein-compounds.

Glutin immersed in cold *water*, becomes soft, swells, and loses its transparency; in warm water it dissolves, forming a colourless, viscid solution, from which, on cooling, it separates as a jelly; Bostock's experiments show that good hard glutin will separate in this manner when diluted with 100 times its bulk of water. After being repeatedly dissolved in hot water, it loses the property of gelatinising. Gelatinised glutin gradually becomes acid on exposure to the air, and then loses its property of fixing and binding. It is perfectly insoluble in alcohol, ether, fats, and volatile oils; on the addition of *alcohol* to its warm solution, it coagulates into a white, tenacious, almost fibrous mass, which, however, readily dissolves again when warmed in pure water.

Acids and *alkalies* throw down no precipitate from aqueous solutions of gelatin; the latter in a dilute state precipitate a little bone-earth. Of the organic acids, *tannic acid* is the only one which throws down a precipitate from a solution of glutin; the precipitate is white and cheesy, and is observable even if the glutin be dissolved in 5000 times its weight of water.

The only *earthy* and *metallic salts* which precipitate glutin are corrosive sublimate, bichloride of platinum, and sulphate of binoxide of platinum. *Ferrocyanide of potassium* does not affect either its neutral or its acid solution *Chlorine, bromine,* and *iodine,* on the other hand, act very powerfully on a solution of glutin; chlorine causes the separation of a coagulum which is partially thready, and after prolonged action, compounds are formed of chlorous acid and undecomposed glutin. *Creosote* gives a milky appearance to the clear solution; the salts of alumina, suboxide of mercury, the oxides of silver, copper, and lead, and of protoxide and peroxide of iron, exhibit no reactions when added to a solution of glutin, or, at most, cause only a very slight turbidity; and the same is the case with basic acetate of lead. *Basic sulphate of binoxide of iron* when added to a solution of glutin, causes a bulky precipitate, which, when dried, is of a deep red colour.

Moist glutin exposed to the air soon undergoes putrefaction; it first becomes sour, but afterwards developes a large quantity of ammonia; according to Gannal,* the gelatigenous tissues are the first of the solid animal structures to become putrid.

Dry glutin when *heated* softens, swells up, evolves an odour of burned horn, does not easily catch fire, and after burning for a very short time, leaves a voluminous, blistered, glistening coal, which after perfect combustion, yields a somewhat varying amount of phosphate of lime. The products of its dry distillation are those of the animal tissues generally; it yields, however, a preponderating quantity of carbonate of ammonia.

When boiled with concentrated *nitric acid,* glutin becomes gradually converted into oxalic and saccharic acids, and into two substances resembling suet and tannic acid. It dissolves in concentrated *sulphuric acid,* forming a colourless fluid, which on boiling gradually yields leucine, glycine, and other substances. If however it be treated with *sulphuric acid and peroxide of manganese or bichromate of potash,* it yields, according to Schlieper† and Guckelberger‡, most of the non-nitrogenous acids of the firs group ($C_nH_{n-1}O_3$), and not only these but valeronitrile, hydrocyanic acid, hydride of benzoyl, benzoic acid, and certain aldehydes, and consequently precisely the same products of decomposition as the protein-compounds; it is however, distinguished from them in yielding even less acetic acid than fibrin, very little benzoic acid and hydride of benzoyl, but on the other hand more valerianic acid than any of the protein-compounds.

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* Hist. de l'embaumement, etc. Paris, 1838

† Ann. d. Ch. u. Pharm. Bd. 59, S. 1-32.

‡ Ibid. Bd. 64, S. 39-100.

When boiled or fused with *hydrated potash* glutin developes ammonia, and is for the most part decomposed into leucine and glycine.

Composition.—Glutin has been analysed by Mulder*, Scherer†, and Goudoever‡. They found it to contain:

	Mulder.	Scherer.	Goudoever.
Carbon	50·40	50·76	50·00
Hydrogen	6·64	7·15	6·72
Nitrogen	18·34	18·32	—
Oxygen	24·62	23·77	—
	10·000	10·000	

No chemical formula that can be depended upon, has been deduced from these analyses. Mulder originally calculated $C_{13}H_{10}N_2O_5$, and Liebig $C_{52}H_{40}N_8O_{20}$, as the most correct formula. The calculations were for the most part based on its combinations with chlorous acid.

Schlieper§ has found 0·12 to 0·14% of sulphur in glutin obtained from bones and ivory.

Preparation.—In order to prepare glutin in the purest possible form from common glue, (which is obtained by boiling skins, tendons, &c., and the swimming-bladder of certain kinds of fish,) Berzelius used to soften it in water, to expose it repeatedly to strong pressure, and then to suspend it in a linen bag in cold water till everything soluble in that fluid was removed. The softened glutin contained in the bag is then heated to 50°, when it becomes perfectly fluid, and must be rapidly filtered. The albuminous and mucous portions remain on the filter, while the hot solution of glutin passes through, and very soon again gelatinises.

In order to prepare glutin from bones, we must digest them for a considerable time in dilute hydrochloric acid, in order to extract the bone-earth, allow the remaining cartilage to lie for some time in pure water in order to remove any adhering hydrochloric acid, and finally boil it with water. Glutin obtained from bones, skins, and tendons, has always a slightly yellow colour.

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* Bullet. de Néerlande. T. 1, p. 23; Ann. d. Ch. u. Pharm. Bd. 46, S. 205-207.

† Ann. d. Ch. u. Pharm. Bd. 40, S. 46-49.

‡ Ibid. Bd. 45, S. 62-67.

§ Ibid. Bd. 58, S. 379-381.

Pure, colourless glutin can only be obtained from cellular tissue, shavings of hartshorn, calves' feet, and the swimming-bladder of certain fishes, by boiling them till they are thoroughly dissolved, filtering them while hot, and removing from them all foreign substances by the method recommended by Berzelius, which has been already described.

Combinations.—On passing *chlorine gas* into an aqueous solution of glutin, each bubble of gas becomes enveloped in a glutinous capsule; the fluid itself becomes milky; white flakes are observed on its surface, and at the bottom of the vessel we observe a deposit of a semi-transparent jelly. The substance which separates at the surface has a frothy, snow-white appearance, is tough and elastic, has a decided odour of chlorous acid, and can be dried at a temperature below 40° without becoming coloured; after it has been partially dried, it may be deprived of all its water at 100°, and then no longer evolves any odour of chlorous acid. In this state the body is white, easily pulverisable, and insoluble both in water and in alcohol. When ammonia is poured over it, nitrogen is developed, and hydrochlorate of ammonia and unchanged glutin are left.

Mulder* found that the action of chlorine and water on the organic substance gives rise to the formation of hydrochloric and chlorous acids, the latter of which enters into combination with the unchanged glutin, the compound consisting of 1 equivalent of acid and 4 equivalents of glutin.

Assuming that the composition of this substance is represented by the formula $C_{52}H_{40}N_8O_{20}+ClO_3$, its atomic weight$=8544{\cdot}26$. Mulder has found two other combinations of glutin with chlorous acid in the above mentioned gelatinous deposit of the solution of glutin; one consisting of 1 atom of glutin with 1 atom of chlorous acid$=C_{13}H_{10}N_2O_5+ClO_3$, and the other of 3 atoms of glutin and 2 atoms of acid$=C_{39}H_{30}N_6O_{15}+2ClO_3$.

The action of *acids* on glutin has on the whole been as yet little examined; with dilute mineral acids it appears to enter into combinations, which, however, on cooling, gelatinise in the same manner as pure glutin. Concentrated *acetic acid* dissolves glutin which has been softened in water, and deprives it of the property of gelatinising on cooling.

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* Bull. de. Néerl. T. 2, p. 152.

The only compound which has been carefully studied is that which it forms with *tannic acid*. This has been done by Mulder, who finds that, when freshly precipitated, it is white and curdy, when dried it is hard, brittle, and pulverisable, and that it is insoluble in water and alcohol. If the glutin is precipitated with an excess of tannic acid, we obtain a combination of equal equivalents of glutin and tannic acid$=C_{13}H_{10}N_2O_5+C_{18}H_7O_{11}$; if, on the other hand, there be an excess of glutin, the precipitate consists of 3 equivalents of glutin and 2 equivalents of tannic acid $=C_{39}H_{30}N_6O_{15}+C_{36}H_{14}O_{22}$.

No combinations of glutin with *alkalies*, *earths*, and pure *metallic oxides* are as yet known. Caustic lime dissolves in a solution of glutin. Glutin can, however, combine with several *basic salts;* a very considerable quantity of freshly precipitated bone-earth dissolves in a solution of glutin. Solutions of glutin, when treated with alum and with sulphate of peroxide of iron, do not yield a precipitate, except on the addition of an alkali; the precipitate in this case consists of glutin and a basic salt$=Al_2O_3.SO_3$ or $Fe_2O_3.2SO_3$. The precipitate obtained with sulphate of the binoxide of platinum appears to contain basic sulphate of binoxide of platinum$=PtO_2.SO_3$.

Physiological Relations.

Occurrence.—Haller's remark: *Dimidium corporis humani gluten est*, now requires to be modified to the assertion that *half of the solid parts of the animal body are convertible, by boiling with water, into gelatin;* for actual gelatin is not contained in the animal organism. It has been for a long time maintained that gelatin is an actual constituent of the swimming bladder of certain fishes; but even this is by no means probable.

The tissues of the human body have been divided into the gelatigenous and the albuminous. Appropriate as such an arrangement might at first sight appear, it is opposed by the experience both of chemists and anatomists; Berzelius and E. H. Weber assert that as the permament cartilages are not converted by boiling with gelatin, and as moreover they cannot be regarded as albuminous, cartilages must be divided into the gelatigenous and non-gelatigenous, and thus these observers abandon the old division of the tissues. Müller has subsequently devoted much attention to the structure and constitution of cartilage, and he finds that the permanent and fibrous cartilages which were previously regarded as non-gelatigenous, may be converted by very prolonged boiling into a gelatinising and gluing substance; but at the same time he ascertained that in many of its other properties, this substance did not coincide with ordinary gelatin; hence he named it *cartilage-gelatin*, or *chondrin*.

Bone-gelatin or glutin is obtained from the following tissues, by boiling them for a longer or shorter time with water; from the cartilages of bone (after ossification), from tendons, the skin, calves' feet, hartshorn, isinglass, the scales of fish, and from the permanent cartilages, when they become ossified by disease. The conversion of these animal parts into glutin proceeds without any development of gas or absorption of air; acids promote this metamorphosis, just as they facilitate many similar transformations in organic chemistry, which can take place by mere boiling without their coöperation, but yet are hastened by their presence, as, for instance, in the case of starch.

We shall revert to this subject when treating of the individual tissues, and of their relation to gelatin.

Origin.—We have already referred to the production of gelatin from the gelatigenous tissues; a comparison of the analyses of pure gelatin with those of the tissues yielding it, will (in a future part of the work) show us that there is no chemical difference between the two, or that at most they only differ by a few atoms of water. Hence it appears that in the formation of gelatin, the material of the tissues only undergoes a re-arrangement of its atoms, or a metamerism, or at most that it only assimilates water, just as occurs when starch, inulin, and lichenin are converted by prolonged boiling into dextrin or glucose.

We shall have occasion to refer in considerable detail to the production of gelatigenous from albuminous matters, when we treat of cell-formation and the history of development.

Uses.—From what has been already said, it follows that we are unable at present to discuss the uses of gelatin in the animal body. The consideration of the tissues from which we obtain gelatin by boiling, pertains solely to histology, and the tissues themselves have as yet hardly fallen within the scope of chemical investigation. We learn from a very superficial consideration of the animal body that the gelatigenous tissues belong for the most part to the lower class of tissues, which are only of use through their physical properties; they frequently afford strong points of attachment for muscles, and furnish strong investments for important but easily injured organs; they give uniformity to the movements of the body through their elasticity, and protect it from the injurious effects of severe concussions; from being bad conductors of heat, they guard the body against rapid changes of temperature; and sometimes, as in the cornea, they are useful as refracting media, in consequence of their transparency.

CHONDRIN.

Chemical Relations.

Properties.—Chondrin or cartilage-gelatin, when dry, appears as a transparent, horny, glistening mass, which is generally more colourless than glutin; it is not rendered electric by friction; its behaviour towards indifferent solvents, towards heat, corrosive sublimate, tannic acid, and chlorine, is precisely the same as that of glutin; but its relations to acids and most metallic salts are quite different. It was shown by Müller* that *acetic acid* throws down a considerable precipitate from a solution of chondrin, and that this precipitate does not dissolve even in concentrated acetic acid. Simon† and Vogel‡ have subsequently proved that most acids throw down a precipitate from a solution of chondrin, but that this precipitate easily escapes notice in consequence of the facility with which it dissolves in a slight excess of the acid. *Alum, the sulphates of the protoxide and peroxide of iron, sulphate of copper, neutral and basic acetate of lead, and the nitrates of silver, and of suboxide of mercury* throw down copious precipitates. The precipitates thrown down by the salts of alumina occur in white, compact flocks, which on drying, cake very much together; they are insoluble in water, but dissolve in an excess of the earthy salt, as well as in solutions of chloride of sodium and of alkaline acetates. The precipitate thrown down by sulphate of peroxide of iron is not soluble in an excess of that salt, but dissolves on boiling. In its relations towards ordinary atmospheric influences as well as towards alcohol, creosote, chlorine, bromine, iodine, and ferrocyanide of potassium, chondrin perfectly resembles glutin. Its combinations with other bodies and its products of decomposition have not yet been accurately studied.

Composition.—Mulder§ was the first who made an elementary analysis of chondrin; he found that besides the ordinary elements of animal substances it contains a little free sulphur, and that it yields more than 4% of an ash consisting chiefly of bone-earth. It has subsequently also been analysed by Scherer* and Schröder†. The following are the results of their analyses:

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* Pogg. Ann. Bd. 38, S. 295.

† Medicin. Chemie. Bd. 1, S. 108.

‡ Journ. f. pr. Ch. Bd. 21, S. 426.

§ Natuur en Scheik. Arch. 1837, p. 450, and 1838, p. 160.

	Mulder.	Scherer.	Schröder.
Carbon	49·97	50·754	49·88
Hydrogen	6·63	6·904	6·61
Nitrogen	14·44	14·692	—
Oxygen	28·59	27·650	—
Sulphur	0·38		
	100·00	100·000	

From these results Mulder constructs the formula $C_{32}H_{26}N_4O_{14}$ and Scherer, $C_{48}H_{40}N_6O_{20}$.

Preparation.—Chondrin is most readily obtained by boiling the cartilages of the ribs, larynx, or joints, for from 18 to 24 hours in water; to purify it we must adopt the same means as are recommended for glutin, and we must extract the dried residue with alcohol.

Physiological Relations.

Occurrence.—The remarks which have been already made regarding the occurrence of glutin in the animal organism, are equally applicable in relation to chondrin. Chondrin does not occur ready formed in the organism, but is produced by the prolonged boiling of certain tissues in water; all permanent cartilages in a healthy state yield chondrin on boiling. Müller's discovery that bone-cartilage not only yields chondrin before ossification, but also sometimes after it has undergone morbid changes, is very remarkable, and shows that chondrin and glutin, notwithstanding their perfectly different constitution, stand in a definite relation to one another; but what that relation is, we cannot at present conjecture.

There are, further, in the animal organism, several bodies which yield a gelatin distinct both from chondrin and glutin. Thus, Müller has shown that in *osteomalacia* where there is sometimes a considerable diminution of the phosphate of lime, the bones yield neither glutin nor chondrin; that the *elastic tissue* of the arteries, by prolonged boiling, yields a kind of gelatin which only differs from chondrin in yielding no precipitate with sulphate of peroxide of iron; that the bones of cartilaginous fishes are converted by boiling into a substance which does not gelatinise but which glues very well, and which, moreover, resembles chondrin in its behaviour to acetic acid and metallic salts, but is not precipitated by the salts of the oxides of platinum, silver, and gold; and, finally, that ossified fish-cartilage when boiled, yields a non-gelatinising fluid which is precipitated by tannic acid, but not by acetic acid and the salts of alumina, and consequently, approximates in its character to glutin.

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* Ann. d. Ch. u. Pharm. Bd. 40, S. 40-51.

† Ibid. Bd. 45, S. 52-58.

Origin.—In our observations on glutin we pointed out that we are still perfectly ignorant of the mode of origin of chondrin. The experiments of Müller render it highly probable that glutin is formed from chondrin. But how? This must be decided by future researches.

Uses.—The animal tissues which yield chondrin are of the same use through their physical properties as those which yield glutin; their most important character being their elasticity.

FIBROIN.

Chemical Relations.

Properties.—It is a white, amorphous mass, devoid of odour or taste, insoluble in water, alcohol, and ether, but dissolving in concentrated sulphuric, nitric, and hydrochloric acids, from which solutions, if diluted with water, it is precipitated by tannic acid; it is insoluble in acetic acid and in ammonia; it dissolves in a concentrated solution of potash but at the same time undergoes decomposition. This substance becomes decomposed, when heated; developing ammonia and empyreumatic vapours.

Composition.—This body was discovered and has been analysed by Mulder[*]; it consists (taking the mean of four of his analyses) of:

Carbon	48·61
Hydrogen	6·50
Nitrogen	17·34
Oxygen	27·55
	100·00

From these numbers Mulder calculated the formula $C_{39}H_{31}N_6O_{17}$ according to which fibroin may be regarded as 3 atoms of glutin which have assimilated 1 atom of oxygen and 1 atom of water, for $3(C_{13}H_{10}N_2O_5)+HO+O=C_{39}H_{31}N_6O_{17}$. Mulder and Croockewit[†] moreover found that the common sponge contains the same substance in combination with iodine, sulphur, and phosphorus; and Mulder considers from the analyses of Croockewit that the compound consists of 20 atoms of fibroin, 1 atom of iodine, 3 atoms of sulphur, and 5 atoms of phosphorus; for there were found in sponge 1·08% of iodine, 0·50% of sulphur, and 1·90% of phosphorus, besides the elements of fibroin.

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[*] Natuur en Scheik. Archief. D. 3, p. 93, D. 5, p. 281.

[†] Scheik. Onderz. D. 2, p. 1.

Preparation.—Silk or gossamer threads are boiled with water and strong acetic acid till all albuminous and gelatinous matters are dissolved. The remaining fibroin is then purified in the ordinary manner.

Physiological Relations.

This substance has hitherto been only found in the above mentioned secretions of silk-worms and spiders; physiological investigations show us that it is originally a viscid fluid which is secreted by the spinning vessels of those animals, and hardens on exposure to the air. Under the microscope the fluid mass appears perfectly amorphous.

Sponge is, as is well known, the dry skeleton of an animal belonging to the *Porifera* (Grant) and named *Spongia officinalis* (Linn.) Its chemical constitution affords one of the arguments why the *Spongia* should be classed amongst animals and not amongst plants, since in the vegetable kingdom we nowhere meet with a substance in the slightest degree resembling fibroin.

The physiology of these lower animals has been so little investigated that it is impossible for us to set up an hypothesis regarding the formation of this substance, for notwithstanding the very accurate analyses of Mulder we cannot be regarded as knowing anything of its intimate chemical composition. Mulder's comparison of the composition of this body with that of gelatin, can indicate nothing more than the analogy in relation to the physiological value of both substances, that is to say, that nature produces in these lower animals a similar group of atoms in order to construct their solid groundwork of tissues possessing little or even no vitality. The use of this substance is therefore purely mechanical.

CHITIN.

Chemical Relations.

Properties.—This substance, to which Lassaigne gave the name of *Entomaderm*, is a white, amorphous body, which usually retains the form of the tissue from which it is prepared; it is insoluble in water, acetic acid, and alkalies, but dissolves in concentrated nitric and hydrochloric acids without communicating any colour to those fluids; after neutralisation with ammonia, tannic acid throws down a precipitate from these solutions. In concentrated sulphuric acid it swells up and becomes dissolved without communicating any change of colour to the acid; it gradually however again separates as a black mass, while acetic acid and acetate of ammonia remain in solution; no sulphurous or formic acid is however formed. It is not decomposed by the most concentrated solution of potash, even at a boiling heat; heated to 280° with water in closed tubes, it becomes brown and brittle without undergoing any change of structure that can be detected by the microscope. There are two points worthy of notice in connexion with the dry distillation of this substance; it does not fuse, but leaves a charcoal which on microscopic investigation always exhibits the form of the original tissue; and further, notwithstanding that it contains nitrogen, it yields acid products of distillation in which not only water and acetic acid are found, but also acetate of ammonia and a little empyreumatic oil.

Composition.—This body has been analysed by Lassaigne[*] and Payen,[†] and has been most carefully studied by C. Schmidt[‡]. Payen found much too little nitrogen. The results of various analyses and experiments which I have made with chitin exactly correspond with those of Schmidt. The following are the results of our analyses.

	Schmidt.	Lehmann.[§]
Carbon	46·64	46·734
Hydrogen	6·60	6·594
Nitrogen	6·56	6·493
Oxygen	40·20	40·179
	100·00	100·000

Schmidt regards $C_{17}H_{14}NO_{11}$ as the simplest formula expressing this composition. He directs especial attention to the peculiar relations of this substance when acted upon by heat and by acids, and arrives at the very interesting result that this body which so closely resembles vegetable bodies and especially vegetable fibre, may be regarded as composed of a carbo-hydrate similar to cellulose, and of a nitrogenous body which has the composition of the muscular fibre of insects. The latter is represented, according to his analyses, by the formula $C_8H_6NO_3$; and $C_{17}H_{14}NO_{11} - C_8H_6NO_3 = C_9H_8O_8$.

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[*] Journ. de Chim. méd. T. 9, p. 379.

[†] Compt. rend. T. 17, p. 227.

[‡] Zur vergleichend. Physiol. der wirbellos. Thiere, 1845, S. 32-69 [or Taylor's Scientific Memoirs, vol. 5, pp. 14-28.—G. E. D.]

[§] Jahresber. d. ges. Med. 1844, S. 7.

Preparation.—The best method of obtaining this body is by boiling the elytra of the cockchafer with water, alcohol, ether, acetic acid, and alkalies; the body always perfectly retains the structure of the elytrum, or of the other insect-tissues from which it is prepared.

Physiological Relations.

This body forms the true skeleton of all insects and crustacea. It constitutes not merely their external skeleton, the scales, hairs, &c., but also forms their tracheæ, and thus penetrates into the minuter portions of the organs; indeed even one of the layers of the intestinal canal of insects consists of chitin; hence we can very well prepare all these parts by treating insects with a solution of potash and then microscopically examine the finest parts, as for instance, the valves of the tracheal openings.

If Schmidt's hypothesis regarding the constitution of chitin be confirmed by further observations, it would be easy to understand how this substance is formed from the food of insects.

In reference to its application in the insect organism, chitin is at most entitled to be regarded as a histogenetic substance.

Before concluding our remarks on the organic substrata of the animal organism we would briefly review the mode of arrangement in which these substances have been considered. We observed in our remarks introductory to the subject of Zoo-Chemistry that the physiological and chemical classifications of animal substances must perfectly coincide with one another; and now in our concluding observations we are constrained to admit that our knowledge of the organic substrata of the animal body is still very deficient, and that we have been provisionally compelled to adopt a practical classification and arrangement, in which, passing from the simpler to the more complex bodies, we have attempted to group together substances presenting chemical similarities with those of equal physiological importance. The deficiency of our knowledge on many points to which allusion has frequently been made, must plead as an apology for the deficiencies in our mode of arrangement. The laborious accumulation of properties, which are only slightly connected or are even altogether inapplicable, has grievously oppressed the science of chemistry, and has reduced it to a mere task of the memory. We have as yet no logical ideas in relation to chemistry ; that is to say, although we have perfectly clear perceptions regarding most bodies and processes, we have no distinct ideas (in the logical sense). There is an utter absence of those principles of unity around which, as around a nucleus, the individual properties of bodies can crystallise, and thus stand in the same mathemathical relation to one another, as the edges and angles of crystal.

It is not till chemistry shall have shown us the close mutual connexion that exists between the properties of all individual substances, and shall have taught us to unite them into one organic whole, that we can regard it as coëqual in scientific rank with the different branches of physics,—that it will fully admit of the application of the higher mathematics,—or that the sole rational principle of classification as well as a scientific theory of chemical substances will be discovered. The beautiful investigations of Kolbe and others regarding the numerical ratio existing between the densities and boiling points of the haloid bases, the volatile acids, and the haloid salts, as also the comparisons of the coefficients of density of the constituent elements with the other properties of the compound substance, may form a small beginning towards the attainment of logical ideas and the realisation of such a degree of chemical knowledge. When we have once attained logical ideas regarding the different animal substrata,—when we are in a position to foretell the chemical properties of a body from its composition, or its composition from a certain number of its properties,—we shall then not only possess the true principle of classification in physiological chemistry, but we shall also have attained the means of investigating and comprehending the vital processes of nutrition and secretion with a degree of certainty at present limited to the most exact sciences.

MINERAL CONSTITUENTS OF THE ANIMAL BODY.

The chemistry of inorganic bodies has been so much more fully investigated than that of organic substances, that it might naturally be expected that our knowledge of the mineral constituents of vegetable and animal bodies would far exceed that of the organic constituents; but, in truth, the reverse is the case, for we are far less acquainted with these substances than with many organic bodies. This circumstance is, however, not consequent on our having paid less attention to the mineral constituents of organic bodies, but is especially owing to the difficulty of separating these substances, in an unchanged state, from organic matters, and of ascertaining the conditions and combinations in which they actually existed preformed in the organic substance. The fixed products of the incineration or combustion of organic substances do not afford us any information as to the combinations in which they occurred in the organic substance. Nor can any reflecting chemist for a moment suppose that the oxides and salts of the ash are contained as such in the juices and tissues of living bodies.

From a deficiency in the means of investigating or even of conjecturing the true constitution of these substances in organic parts, a higher value has been attached to the determinations of the ash and its constituents than it merited, and the results of these analyses have been more highly estimated than they deserve, when we consider the agents coöperating in the incineration. It has, moreover, frequently been forgotten that the quantity and constitution of many of the constituents of the ash are in a great measure dependent on the height of the temperature at which the process of incineration was conducted; that a great portion of the substances has been volatilised by the simultaneous action of heat and carbon; and that the individual constituents of the ash have entered into perfectly different combinations from what they had done in the organic substance.

We will here indicate only some few of the changes which the mineral constituents of organic substances must necessarily undergo when exposed to strong heat with a free admission of air. The sulphur and phosphorus which were not contained in the organic substance as sulphuric and phosphoric acids, must necessarily be found in the ash as sulphuric and phosphoric acids combined with bases; and although this necessary change has not been overlooked, the consequences have too often been neglected. When in the first place we direct our attention to the sulphuric acid, we shall find that the number representing this acid as found in the ash, can scarcely ever correctly express the quantity of sulphuric acid existing preformed in the organic substance, or the sulphur contained in it. For if we suppose all the sulphur converted by combustion into sulphuric acid, and united to the bases that had previously been combined with organic substances or with carbonic acid, a great portion of the sulphur must be lost, even when these bases are sufficient for the saturation of the sulphuric acid that is formed (which is not always the case, as, for instance, in the bile) in consequence of the sulphates in contact with the nitrogenous charcoal, which is so difficult of incineration, being converted into metallic sulphides, of which a larger or smaller quantity will escape as sulphurous acid during the prolonged process of calcination. Under the action of a strong glowing heat common phosphate of soda removes a part of the base, not only from the carbonates, (see p. 97,) but also from sulphates of the alkalies, as well as from the metallic chlorides of the ash, so that not only does all the alkaline carbonate disappear from the ash, but a portion of the hydrochloric or sulphuric acid may be also lost. Where the ash contains acid phosphate of soda, as occasionally happens in urine devoid of lactic acid, a portion of the phosphoric acid must necessarily be lost; for we know with what difficulty carbon burns in the presence of fusible salts, and it must be recollected that a portion of the phosphoric acid of the acid salts will be reduced by the carbon and volatilised. These few remarks may suffice to show how little atttention was formerly directed to the reciprocal decompositions experienced by the mineral salts that occur in vegetable or animal substances, under the influence partly of a simple glowing heat, partly of heat in the presence of unconsumed carbon, and partly of a glowing heat in oxygen gas.

I have endeavoured in some degree to evade these obstacles in the way of the determination of the mineral constituents of animal bodies, by isolating organic substances as much as possible, according to their solubility (as I have done in the case of blood,* for instance,) and then determining the constituents of the ash of each separate extract; by which means we may be justified in expecting that the soluble salts that are preformed in the blood will be contained in the aqueous and alcoholic extracts, and that the presence of organic substances, owing to their inconsiderable quantity in these extracts, will exert less influence on the decomposition of the salts during incineration. In order as much as possible to avoid the influence of the carbon and of the phosphates, during the process of incineration, on the carbonates, I have been in the habit of not exposing the whole of the carbonaceous residue originally obtained from the organic substance to entire combustion, but of reducing it to a small bulk over a gentle fire with free access of air. The carbonaceous ash is then extracted with water and hydrochloric acid, and the quantitative determination of the ash is obtained by weighing and subtracting the residuary charcoal. But, although I have certainly obtained more correct results by this method than those yielded by the majority of previous analyses of ash, it is nevertheless not free from error, nor can it be said to afford an entirely satisfactory insight into the nature of the mineral substances existing preformed in animal bodies. Fortunately for science, H. Rose*, one of the most distinguished analysts of our day, has entered upon this hitherto unpromising subject, and by a series of the most carefully conducted investigations has obtained important results, which are in part of a purely physiological character. One of the most important facts ascertained by these successful researches in analytical chemistry is, that in the animal or vegetable substance perfectly carbonised by heat, there is usually a greater or lesser quantity of alkaline and earthy salts, which cannot be removed from the carbonaceous mass, even by the most prolonged extraction either with water or acids. These mineral substances must therefore be contained in the carbonised residue in a different condition from those which admit of being removed by various menstrua. Rose, therefore, concludes that such substances as alkalies, earths, metals, phosphorus, sulphur, &c., must be contained in the carbonaceous mass in a non-oxidised state, and in combinations with which we are still unacquainted: he also thinks that it may be assumed that such combinations of potassium, sodium, calcium, iron, phosphorus, and sulphur, also exist preformed in organic substances, since on the one hand the carbonisation of organic substances free from ash (as for instance sugar) with the ordinary constituents of the ash did not yield any carbonaceous residue that could not be perfectly freed by the ordinary menstrua from mineral substances; and since, on the other hand, we are already acquainted with some organic bodies in which we assume that non-oxidised sulphur or non-oxidised iron is present in a peculiar state of combination. Hence Rose further concludes that in vegetable and animal substances those mineral constituents can alone be regarded as preformed, which admit of being extracted by means of water and acids from the carbonised material, while on the other hand those substances which cannot be separated until the carbonaceous mass is entirely burned, are inherent in the original organic substance, as integral constituents in a non-oxidised condition.

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* Berichte der k. sächs. Gesellsch. d. Wiss. Bd. 1, S. 98.

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* Pogg. Ann. Bd. 70, S. 449-465, Berichte der Akad. der Wiss. zu Berlin, Decbr. 1848, S. 445-462, and Pogg. Ann. Bd. 76, S. 305-404. [The last of these memoirs is translated in the London, Edinburgh, and Dublin Philosophical Magazine. New series, vol. 35, pp. 1, 171, and 271.—G. E. D.]

It appears from the numerous investigations prosecuted by Rose, with vegetable and animal products, that while there are some, as, for instance, the bones, in which all the mineral constituents are in a perfectly oxidised state, that is to say, admit of extraction by the ordinary solvents, (and these he names *teleoxidic* organic substances,) the great majority contain the mineral constituents partly in an oxidised and partly in an unoxidised state (these he terms *meroxidic*), while none are as yet known that contain only unoxidised elements (*anoxidic*.)

In his examination of vegetable substances, Rose found that the straw of different kinds of grain was almost perfectly *teleoxidic*, whilst the seeds of the same plants were *meroxidic*. In reference to animal substances, it was to be expected that, as the meroxidic substances belonging to the vegetable kingdom specially serve as food for the animal organism, those animal fluids and tissues whose chemical constitution approximates to that of vegetable substances, as the blood, the muscular fibre, milk, and yolk of egg, would be meroxidic, whilst the excretions, as matters which originated in the animal body mainly by the process of oxidation, would be teleoxidic. This supposition has been fully confirmed by the analyses of the bile, the urine, and solid excrements, instituted by Weber, Fleitmann, Weidenbusch, and Poleck. In order to take a general view of these relations, we will subjoin the numerical results which have been obtained, according to Rose's method, by investigations on the mineral constituents of animal substances. In the following table, A represents the quantity of the salts that can be extracted by water from 100 parts of the mineral constituents of the organic substance; while B represents the quantity of salts dissolved by hydrochloric acid; and C, the quantity of the salts which can only be determined by the combustion of the carbonaceous residue.

	A.	B.	C.
Ox-blood	60·90	6·04	33.06
Horse-flesh	42·81	17·48	39·71
Cows' milk	34·17	31·75	34·08
Yolk of egg	40·95	8·05	51·00
White of egg	82·19	15·52	2·29
Ox-bile	90·85	4·93	4·22
Urine	90·87	8·54	0·59
Solid excrements	18·55	62·30	19·15

The column C exhibits, therefore, those mineral substances in the oxidised state which, according to Rose, are not oxidised in the organic substance.

It must be further observed, that in the solid excrements the number representing the mineral substances that cannot be extracted, would not be so strikingly high if sand and the silica of the vegetable tissue were not mixed with them; the number representing the non-oxidised substances is also increased in the white of egg, the ox-bile, and the urine, by the silica occurring in them.

Although Rose's investigations have greatly contributed to our advance towards the knowledge of the inorganic constituents of animal substances, we dare not flatter ourselves that we have as yet attained the object in view, for it not only remains for us to apply this method to the investigation of the mineral substances contained in different normal and morbid animal juices and tissues, but also, by further investigation, definitively to determine the question that has been started against Rose's view of the combination of radicals containing sulphur and phosphorus with metals; in other words, it will be necessary to collect a greater number of facts, in order to illustrate this obscure subject in various points of view, before we venture to apply it, in all its consequences, to scientific questions. Yet it cannot be denied that no previous method affords us so good a guide as Rose's, for the correct recognition of the mineral substances existing preformed in organic bodies.

When, however, we have obtained by Rose's method such an admixture of mineral bodies as we may assume to exist preformed in the organic substance, the actual analysis still remains to be made; and this, notwithstanding the labours of the most eminent chemists, has by no means attained to the degree of perfection which has been generally obtained in mineral analyses. The recent investigations of Fresenius, Erdmann, Mitscherlich, and more especially of Rose, have made us acquainted with numerous deficiencies which attached to the former methods of examining the ashes of vegetable and animal substances; and notwithstanding this, we are struck with the great accuracy of many of the earlier analyses of ashes, although from the methods then employed we should have expected that their calculations would of necessity have yielded a *minus* in the one case and a *plus* in the other.

We will here only refer to the fact that few observers before Rose had observed that alkaline as well as earthy salts were contained in the insoluble portion of the ash, and that, conversely, the presence of carbonate and phosphate of lime in the aqueous extract of the ash had been very generally overlooked, while the very imperfect precipitation of the pyrophosphate of magnesia by ammonia was equally disregarded. The imperfect manner in which even the simplest relations of this nature have been investigated, is made apparent by the doubts entertained by Berzelius himself, in reference to the composition he had ascribed to bone-earth, which were verified by the investigations of Rose and W. Heintz,[*] by whom it was definitely proved that the phosphate of lime in the bones is represented by $3CaO.PO_5$, and not as Berzelius had given it, by $8CaO.3PO_5$. The difficulty of conducting exact analyses of ash was, however, mainly increased by the deficiency of any clear and comparatively simple method of separating phosphoric acid from its proteus-like salts, and determining it quantitatively. But this cause of difficulty has likewise been recently obviated by H. Rose's[†] method of thoroughly separating the acids from their bases by means of mercury and nitric acid.

When we consider these facts in reference to the analysis of the ash, we shall readily arrive at the conclusion, (without, however, wishing to animadvert upon those analysts who have engaged in laborious examinations of the ash of animal bodies,) that most of these analyses should be used with great caution, and that physiological conclusions should not be too readily drawn from them. It has, unfortunately too often happened that the empirical results of analyses of the ash have been applied to the explanation of physiological processes without due consideration, and thus the importance and efficiency of the mineral salts of the animal body have been extolled before we had any accurate knowledge of the substances themselves; and the most rigorous scepticism in reference to medical experiments has not unfrequently been associated with a blind confidence in the least reliable of the numerical determinations of chemists.

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[*] Ber. der Ak. d. Wiss. z. Berlin, Febr. 1849, S. 50-53.

[†] Ibid. S. 42-45.

Since we have made a practice of incorporating the methods of qualitative and quantitative analysis in the description of the organic substrata, it might naturally be expected that we should in like manner enter into a special consideration of the different methods for analysing the ash; but however important this subject may be, both in itself and in reference to physiology, we have, nevertheless, been deterred by many reasons from adhering to this rule in the present case. Thus, for instance, if we were once to enter thoroughly within the domain of inorganic chemistry, we should far exceed the limits assigned to this work, more especially if we were definitely to refer to, and critically to illustrate, the different methods for the analysis of the ash and the determination of individual constituents; nor could we indicate any one method as the best, since different objects demand different methods. We, moreover, entertain the frequently expressed but rarely practised view that the study of physiological as well as of organic chemistry generally, should be based upon an exact knowledge of inorganic chemistry in all its relations, for many of the deficiencies which we have found occasion to notice in the researches of zealous physiological and pathological chemists are referable to an inadequate knowledge of inorganic chemistry. We are, therefore, the more resolved to omit all notice of the analyses of mineral substances, again referring our readers to the admirable memoirs which have appeared in recent times on this subject, and for which we are indebted to Will and Fresenius,* Mitscherlich,† Knop,‡ Erdmann,§ Heintz‖, Rose¶, [and Strecker.**—G. E: D.]

If we venture to adopt a physiological classification in our description of the mineral substances of the animal body (which, moreover, can refer only to their physiological function,) we adopt this course simply from a feeling of its great applicability, and not because we consider ourselves able to indicate the exact place occupied in this system by each individual mineral substance; for the remarks we have already made, must sufficiently indicate the uncertainty and deficiency of our knowledge on this subject. We therefore attempt to divide the mineral substances of the animal body in reference to their physiological importance, into:

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* Ann. d. Ch. u. Pharm. Bd. 50, S. 363-396.

† Ber. d. Akad. d. Wiss. z. Berlin, 1845, S. 236-252.

‡ Journ. f. pr. Ch. Bd. 38, S. 14-47.

§ Ibid. Bd. 38, S. 40-69, and Ber. d. Gesellsch. d. Wiss. zu Leipzig, 1847, S. 83-90.

‖ Op. cit.

¶ Op cit.

** Ann. d. Ch. u. Pharm. Bd. 73.

1. Those which are of especial use in the animal body through their physical properties.
2. Those which are adapted by their chemical properties to serve definite objects in the animal economy: and
3. Those which are only incidentally conveyed into the animal body, exert no influence on any special process, and are, therefore, speedily eliminated from the organism.

First Class of Mineral Bodies.

Water.

It would be superfluous to enumerate the uses of this substance in the animal organism; we will confine ourselves to the two simple remarks that water is essential to the establishment of all chemical activity, and, further, that the functions, or rather the physical properties, of certain tissues, are dependent on the presence of a certain quantity of water which is merely in a state of mechanical combination.

Phosphate of Lime.

This is the most important of all the mineral substances which, by their physical properties, are of service in the animal body. The use of its presence in the bones, where it gives solidity and strength to the osseous skeleton, is at once apparent. Bones deficient in this salt are proportionally deficient in firmness: thus we observe that softening of the bones occurs in those conditions when the animal organism does not receive a sufficient supply of phosphate of lime, or when certain physiological processes require an increased consumption of this salt, as in pregnancy, and during the dentition of children. We need hardly remark that rachitis frequently, if not always, occurs simultaneously with the period of dentition, that the consumption of phosphate of lime during pregnancy is often so great that scarcely any traces of it can be found in the urine, and that during this period of woman's life fractures unite with extreme difficulty, and sometimes do not unite at all. Chossat[*] was able to induce softening of the bones artificially in animals, when he restricted them to food containing little or no phosphate of lime. The permanent cartilages only ossify in old age, when a superabundance of calcareous salts is deposited in them. In the dense, cortical portion of bones, we find more bone-earth deposited than in the spongy parts. The teeth, whose utility depends entirely on their hardness, contain a larger proportion of phosphate of lime than any other part of the animal body; and it exists in still greater quantity in the enamel than in the dentine.

We have previously had occasion to remark that Berzelius, even to a recent time, adhered to the formula $8CaO.3PO_5$ for the phosphate of lime of bone-earth, and that on the other hand the investigations of W. Heintz under Rose's direction, indicate that the formula for the composition of bone-earth should be $3CaO.PO_5$. Berzelius[†] has in part given the reason for his formula. It is not always $8CaO.3PO_5$ which is precipitated from acid solutions containing lime and phosphoric acid, as he formerly assumed; but when there is an excess of lime, and under the prolonged action of caustic ammonia, the basic salt $3CaO.PO_5$ is precipitated. Since the phosphate of lime is for the most part separated in this way, and the lime which is precipitated after the removal of the phosphate is calculated as if it were a carbonate, without any direct determination of the carbonic acid, there must be some uncertainty in the ordinary analyses of the earthy constituents of the bones, in part owing to the not very accurate determination of the magnesia. Heintz has found that this is the composition of phosphate of lime not only in normal human bones, but also in those of the sheep and the ox. In this point of view, however, the investigation of diseased bones requires a thorough revision; moreover, von Bibra's[‡] analyses seem to show that in the teeth the ratio of the phosphoric acid to the lime is not in accordance with either of the above formulæ.

In healthy human bones the phosphate of lime ranges from 48 to 59%; in softening of the bones it may sink to 30%. It is, however, singular that in almost all diseases of the bones, whether the results of osteoporosis, osteomalacia, or osteopsathyrosis, we find a diminution of the phosphate of lime. Even in consecutive induration (or eburneation) the bones often do not regain their normal quantity of phosphate of lime.

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[*] Gaz. méd. 1842, p. 208.

[†] Ann. d Ch. u. Pharm. Bd. 53, S. 286-289.

[‡] Chem. Unters. üb. Knocken u. Zähne. Schweinfurt, 1844, S. 284-287.

Von Bibra has very fully investigated the composition of the different bones of the same individual, and has made the beautiful observation that those bones which are the most exposed to mechanical influences contain the largest amount of earthy constituents. The action of this law is manifested even in different families of the same class of animals; thus, for instance, in the rasores or scraping birds, the femur contains the largest quantity of phosphate of lime, in the grallatores or waders, the tibia, and in all other birds, the humerus.

That the phosphate of lime and the earths generally are only mechanically deposited in the bones, is obvious from the circumstance that we can so thoroughly deprive them of all mineral constituents by dilute hydrochloric acid, that they leave scarcely a trace of ash.

It has for a long time been a matter of discussion whether the phosphate of lime is, or is not, chiefly deposited in the bone-corpuscles and the *canaliculæ chalicophoræ*. I am however now convinced that the dark colour of these parts in refracted light, and their white colour in reflected light, essentially depends on their containing air. Any one may readily convince himself that this is the case, by treating one thin section of bone with dilute hydrochloric acid, so as to remove the earths, and another with a dilute solution of potash, so as to remove the cartilaginous substance, and comparing the two under the microscope. Frerichs* attempted to demonstrate that the earths were uniformly distributed throughout the bone by showing that osseous laminæ from which the cartilaginous substance had been removed by a dilute solution of potash received an uniform yellow tint on the addition of nitrate of silver, and that the bone-corpuscles were not distinguished by any special depth of colour.

Phosphate of lime also occurs in many other parts of the animal body, although in far less quantity than in the bones; indeed there is no animal tissue, in whose ash, on incineration, we do not find phosphate of lime.

Liebig† regards the insolubility of certain tissues, as for instance, muscular fibre and cellular tissue, as partially due to the bone-earth which they contain. In the transition of the blood into these tissues its protein-compounds part with the soluble phosphate of soda but retain a large quantity of the phosphate of lime. It is thus that Liebig accounts for the special power which hydrochloric acid possesses of dissolving these substances during the process of digestion.

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* Ann. d. Ch. u. Pharm. Bd. 43, S. 251.

† Ibid. Bd. 50, S. 170.

Well dried muscular fibre contains, according to von Bibra, from 0·938 to 1·008% of bone-earth.

Phosphate of lime is found in solution in all the animal fluids; its presence has long been recognised in the blood, the urine, the fluids of serous membranes, the saliva, gastric juice, milk, and seminal fluid, but it was for a long time unknown by what means this insoluble body was retained in solution in alkaline and neutral fluids. As a general rule phosphate of lime is chemically combined wtih the protein-compounds and similar organic matters, and is retained by them in their solutions as well as in their metamorphoses into the tissues. Moreover it has been long demonstrated by Berzelius and Thenard, that phosphate of lime is to a certain degree soluble in fluids containing much carbonic acid; we know from analytical chemistry, that it is not altogether insoluble in fluids containing hydrochlorate of ammonia, and recently Liebig has shown that a little phosphate of lime is taken up by solutions of chloride of sodium. The solubility of bone-earth in animal fluids is thus sufficiently intelligible.

We have already spoken of the solvent power which lactic acid exerts on phosphate of lime. In opposition to the experiments of Walter Crum† I will only remark that in my experiments (taking the mean of six) 68·55 parts of basic phosphate of lime were dissolved by 100 parts of anhydrous lactic acid, while a fluid containing 100 parts of anhydrous acetic acid could only dissolve 17·49 parts of the same salt.

The ash of the protein-compounds consists for the most part of phosphate of lime; Berzelius‡ found 1·8% in the albumen from the serum of ox-blood, while Mulder found 2·03% and Marchand from 2·1 to 2·5% in that of the egg; in soluble albumen precipitated by great dilution and neutralisation, I found 1·3% of phosphate of lime; in well-washed fibrin from the venous blood of a man, I found only 0·694%. Casein, globulin, chondrin, and glutin also contain phosphate of lime as an integral constituent. Casein, according to Mulder§ contains 6% of phosphate of lime, which, when the casein is coag-

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* Ann. de Ch. u. Pharm. Bd. 61, S. 128.

† Ibid. Bd. 63, S. 394 ff.

‡ Lehrb. d. Ch. Bd. 9, S. 35.

§ Archiv. f. 1828, p. 155.

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[illegible] u. Physiol. 1839, S. 306.

nated, is precipitated with it, even when there is a sufficient quantity of free acid in the fluid. Chondrin, according to Mulder, yields on incineration 4·19% of ash, most of which is phosphate of lime. As chemical compounds of phosphate of lime with albumen and with gelatin have been prepared, which contain much greater quantities of this salt (in albumen even one-third), there would be nothing absurd in the supposition that a portion of the phosphate of lime contained in the bones, is chemically combined with the cartilaginous substance, even though it may be removed by hydrochloric acid.

The constant occurrence of phosphate of lime in the histogenetic substances, and especially in the plastic fluids, as well as its deposition in many pathologically degenerated cells of the animal body, obviously strengthen the opinion that this substance plays an important part in the metamorphosis of the animal tissues, and especially in the formation and in the subsequent changes of animal cells. This subject must, however, be more fully investigated, before we can draw any definite conclusions regarding it.

In connexion with this subject, C. Schmidt* has, however, made a very interesting observation regarding the folds of the mantle of *Unio* and *Anodonta*. They consist of a middle layer of fibres of areolar tissue, which on its inner side is covered with ciliated epithelium and towards the shell with glandular epithelium; in these parts he found about 15¼ of phosphate of lime, 3¾ of carbonate of lime and soluble salts, and 52¼ of organic matter,—the quantity of phosphate of lime being very extraordinary, as the blood of these animals contains only 0·034¼ of this salt. The mucus, lying between the shell and the mantle of these animals, and secreted by the layer of glandular cells on the mantle for the consolidation of the shell, consists of a strong basic albuminate of lime containing only a little preformed carbonate of lime. Schmidt is of opinion that the function of this glandular epithelium, which resembles the cells of the liver, is to secrete from the blood a combination of albumen and lime, decomposable by the carbonic acid of the air or of water, for the formation of the shell, while it leaves the phosphate of lime for those organs which require it for the process of cell-formation (the testicle and ovary.)

The questions now arise, how do such masses of phosphate of lime find their way into the animal body? Or how are they formed in it? That carnivorous animals receive a more than sufficient quantity with their food is obvious from the preceding observations. Graminivorous animals likewise receive in their food a sufficient quantity of this earthy salt; for in the vegetable kingdom, we find certain nitrogenous bodies which, like the protein-compounds of the animal organism, always contain some phosphate of lime, as for instance, vegetable albumen, legumin, and gluten.

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* Zur vergleichenden Physiol. S. 58-60.

Phosphate of lime, is, however, also formed within the animal organism. If the experiments of von Bibra, showing that the bones of young creatures contain relatively more phosphate of lime than those of older ones, appear to be opposed to the view that the phosphate of lime is formed from the carbonate, the numerous analyses of Valentin* prove that newly formed bones, or parts of bones, always contain a greater quantity of carbonate of lime before they are provided with their proper quantity of phosphate of lime. If we review the different substances taking part in the metamorphosis of the animal tissues, it appears, as a necessary conclusion, that phosphate of lime must be formed from its proximate constituents. We know that several animal substances contain phosphorus in an unoxidised state, and that they are not removed from the organism till they are perfectly decomposed, that is to say, till they are partially oxidised; in this process the phosphorus must be converted into phosphoric acid. We further know that very many animal substances also contain sulphur, and in their decomposition in the animal body form not only sulphuric acid, but also uric, hippuric, and other acids, which must partially decompose the alkaline phosphates that find their way into the body from without, that is to say, by the seeds of the cereals and leguminous plants, so that the liberated phosphoric acid must combine with the lime which enters the animal body with the vegetable food or with the water used as drink. We have an opportunity of almost directly observing the process of the new formation of phosphate of lime from its proximate constituents in the development of the chick within the egg; for the observations of Prout and Lassaigne show that during incubation, such a quantity of carbonate of lime is transferred from the shell of the egg to the yolk, that the augmentation of the phosphate of lime with the growth of the chick during incubation, is not more than can be accounted for.

Valentin's opinion is based on the following observations:—In the carious tibia of a man, aged 38 years, he found 44·12% of ash containing 77·93% of phosphate, and 15·04% of carbonate of lime, while the tibia of a healthy man of the same age yielded 61·98% of ash, in which were contained 84% of phosphate, and 12·8% of carbonate of lime. Hence, in this case, the amount of ash was diminished almost solely at the expense of the phosphate of lime. In the callus, as well as in the exostosis of a horse, he found the carbonate of lime increased in relation to the phosphate, and hence concluded, that, as a general rule, imperfectly formed bones always contain more carbonate of lime than normal bones. Lassaigne's experiments* accord with those of Valentin. In the osteophyte occurring on the inner layer of the skull during pregnancy, there is also much carbonate of lime, as was observed by Kühn; I found 52·46% of organic matter, 30·69% of phosphate of lime, 1·09% of phosphates of magnesia and iron, 0·98% of soluble salts, and 14·78% of carbonate of lime in one of these osteophytes.

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* Repert. f. Anat. u. Physiol. 1839, S. 306 ff.

Prout† was the first who observed that during the incubation of the egg the quantity of phosphorus in its contents remains constant, but that the quantity of lime undergoes a considerable augmentation; he was almost inclined from this observation to conclude that there was a formation of lime from other materials, since he did not regard it as probable that the non-vascular *membrana putaminis* could transfer lime from the shell to the embryo. But if we take into consideration that during incubation the shell experiences a loss both in weight and firmness, and that a part of this *membrana putaminis* becomes dried, and consequently impermeable, while, however, the greater part is in contact with the contents and thus remains moist, it is very easy to perceive that the increase in the amount of lime within the egg arises from its most proximate source, namely, from the shell itself. The phosphorus exists chiefly in the yolk, where it occurs as glycero-phosphoric acid, which during incubation is gradually decomposed, so that the liberated phosphoric acid unites with lime which passes over by endosmosis from the shell into the egg to form this salt. There is, however, so much phosphorus contained in the yolk of the egg, that on incineration it forms acid phosphates, or rather metaphosphates ($NaO.KO.PO_5$), with the bases which it there encounters.

CARBONATE OF LIME.

This salt is principally found in the skeletons of invertebrate animals; but it always occurs, as has been already mentioned, in reater or smaller quantities, in the bones of the vertebrata. Its uses in the animal organism are the same as those of phosphate of lime

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* Journ. de Chim. méd. T. 4, p. 366.

† Phil. Trans. 1822, p. 365.

There can be no doubt that the carbonate of lime found in animal substances is very often no educt, but the product of the incineration to which we have submitted the substance in the course of the chemical analysis; it not unfrequently, however, occurs in the bones of the vertebrate animals as true carbonate of lime, and in the lower classes of this great division we find it deposited in various places in microscopic crystals. Carbonate of lime in considerable quantity is found in the urine of graminivorous animals, in the saliva of the horse, and in many animal concretions.

Numerous experiments have been instituted, especially by Lassaigne, Fernandes de Barros*, Valentin†, and von Bibra‡, with the view of ascertaining the ratio in which the carbonate of lime stands to the phosphate in the bones of different men and animals. According to my own investigations, this ratio in a new-born child = 1 : 3·8, in an adult male = 1 : 5·9, and in a man aged 63 years = 1 : 8·1 ; according to Valentin it = 1 : 8·3 (on an average) in caries, and = 1 : 5·54 in callus, or 1 : 5·3 according to Lassaigne; in an exostosis it = 1 : 52 according to Valentin, and 1 : 1·214 according to Lassaigne; according to Barros it = 1 : 3·8 in the lion, 1 : 4·15 in the sheep, 1 : 8·4 in the hen, 1 : 3·9 in the frog, and 1 : 1·7 in a fish. According to Lassaigne this ratio = 1 : 3·6 in the teeth of a new-born child, 1 : 5·3 in those of a child aged six years, 1 : 6 in those of an adult, and 1 : 6·6 in those of a man aged 81 years.

Von Bibra, in his numerous analyses of bone, has arrived at opposite results, since he found that the bones of young creatures for the most part contained less carbonate of lime than those of older ones. As we must refer for fuller information to von Bibra's work, we shall here only give the quantity of carbonate of lime which he found in the femur in different classes of animals; in the order *glires*, it amounts to 9·48%, in the *ruminantia* to 9·86%, in the *pachydermata* to 10·15%, in the *cetacea* (the dolphin) to 9·99%, in the *pinnipedia* (the seal) to 7·23%, in the *falculata* to 6·26%, in the *pollicata* to 9·18%, and in men to 8·59%.

The urine of graminivorous animals often contains so large a quantity of carbonate of lime as to cause a deposit very soon after its emission. My investigations tend to show that in the urine of the horse carbonate of potash and carbonate of lime very frequently replace one another; I have usually found that urine rendered turbid by the presence of much carbonate of lime contains a very small quantity of alkaline carbonates, and often has only a very slight reaction on turmeric paper, while clear urine is usually rich in alkaline carbonates. Hence it is easy to see why urinary calculi consisting of carbonate of lime are of very common occurrence in herbivorous animals.

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* Journ. de Chim. méd. T. 4, p. 289.

† Op. cit.

‡ Op. cit.

Carbonate of lime sometimes also occurs in human urine with an alkaline reaction; and indeed sometimes, although very rarely, we meet with human urinary calculi, consisting for the most part of carbonate of lime. Proust* was the first who made this observation; but similar calculi have been since found by Cooper, Prout,† Smith, Göbel,‡ and Fromherz.§

In animal concretions, we sometimes find considerable quantities of carbonate of lime deposited with the phosphate. Thus, Geiger found 21·7 of carbonate and 46·7 of phosphate of lime in a nasal concretion; I found 24·3% of carbonate and 69.7% of phosphate of lime in a phlebolith, and Schlossberger¶ 8·3 of carbonate and 50·4 of phosphate of lime in a similar concretion; Walchner** found 23% of carbonate and 50% of phosphate of lime in a concretion from the heart of a man with hydrothorax, and John†† found 66·7% of carbonate and 25% of phosphate of lime in a concretion taken from a stag's heart. Some stony concretions from the peritoneum of a man were found by Bley‡‡ to contain 34% of carbonate and only 19·32% of phosphate of lime; Lassaigne§§ found 83·36% of carbonate of lime in a salivary concretion from a horse. I need hardly advert to the frequency with which we meet with tolerably large quantities of carbonate of lime in the microscopico-chemical investigation of indurated or ossified tumours, as for instance, chalky tubercle.

Carbonate of lime in the crystalline state is very rarely found in the human organism: the only place where it constantly occurs in the normal state is the *utriculus* of the membranous vestibule‖‖ of the inner ear, on whose outer and upper walls it is deposited in minute crystals amongst organic matter. These crystals are usually so very minute, that distinct molecular motion may be observed amongst the smallest of them. The form of the crystals is never a pure rhombohedron, but always a prism derivable from the rhombohedron of calc-spar, most frequently resembling the so-called *Kanonendrusen* of calc-spar;* that is to say, they are six-sided with 3-planed acuminations. Krieger† has also seen twin crystals of the scaleno-octahedral form. Crystals of this nature occur much more frequently and abundantly in the lower animals, both in the organs of hearing and in other parts; perhaps the best known and most striking case of the occurrence of such crystals is in the membrane of the brain of the *batrachia*, and in the white, silvery saccules at the intervertebral foramina through which the spinal nerves emerge. In morbid formations in the human organism, we not unfrequently meet with crystalline deposits of carbonate of lime, which however usually appears rather in irregular crystalline masses, such as are described by Vogel,‡ than as perfectly formed crystals.

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* A. Gehlen's Journ. Bd. 3, S. 532.

† Thomson's Annals of Philos. vol. 15, p. 436.

‡ Trommsdorf's n. Journ. Bd. 9, S. 198.

§ Schweigg. Journ. Bd. 46, S. 329.

‖ Mag. f. Pharm. Bd. 21, S. 247.

¶ Ann. d. Ch. u. Pharm. Bd. 69, S. 254.

** Mag. f. Pharm. Bd. 19, S. 152.

†† Chem. Schriften. Bd. 5, S. 155.

‡‡ Arch. d. Pharm. Bd. 20, S. 212.

§§ Journn. de Chim. méd. 1845. p. 523.

‖‖ [It occurs also in the *sacculus*, and is sometimes scattered in the cells lining *ampullæ* and semi-circular canals.—G. E. D.]

There are obviously two ways in which we may account for the presence of carbonate of lime in the animal organism. It is well known that spring water holding carbonic acid in solution, usually contains a considerable quantity of carbonate of lime; and this might sufficiently explain the presence of this salt, even if it were not in a great measure formed within the organism from other salts of lime, which find their way there in abundant quantity with the vegetable articles of food; hence it is that the urine of herbivorous animals is often so rich in carbonate of lime.

The solubility of this salt in the animal fluids, might, at first sight, seem to be less easily understood than its origin. The free carbonic acid which, it is almost certain, may be detected in all the animal fluids, doubtless acts as a solvent for the carbonate of lime; and I may remind any who may not be satisfied with this explanation, that the old experiments of Guiton Morveau, show that carbonate of lime is also slightly soluble in solutions of the alkaline salts, as for instance, chloride of potassium. Moreover, it is not improbable that there are several animal substances which, like sugar, exert solvent action on carbonate of lime.

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* [The term *Kanonendrusen* is used in the Hartz to signify a crystalline modification of calc-spar. *Drusen* signifies a cluster of crystalline substances. A crystal is said to be *drusy* (*drusig*) when it is coated with a number of minute crystals of the same kind, so that the new surface acquires a scaly aspect. G. E. D.]

† De otolithis. Berolini, 1840, p. 15.

‡ Icones histol. path. Tab. 22, fig. 8.

Phosphate of Magnesia.

Phosphate of magnesia always occurs in such small quantity that we feel scarcely justified in ascribing to it simply a mechanical use in the animal body, and in arranging it in this class of the mineral substances; it is, however, so constantly associated with the corresponding lime-salt that we feel compelled to notice it in this place. Like the phosphate of lime, it is in the osseous system that it is chiefly deposited.

The bones of carnivorous animals and of man contain very little phosphate of magnesia; those of herbivorous animals rather a larger quantity. Berzelius found 1·16% in a piece of human bone, and 2·05% in the bones of an ox; Valentin found 1·943% in a portion of one of the ribs of a horse; Berzelius 1·5% in the enamel of a human tooth, and 3% in that of the tooth of an ox; in human dentine he found 1%, and in that of the ox 2·07%. The numerous analyses of von Bibra afford a general confirmation of these facts; he observed, moreover, that the teeth of the *pachydermata* were especially rich in phosphate of magnesia. Various physiological relations (age, &c.), as well as morbid conditions, augment and diminish the quantity of this salt, which seems, however, to vary in a direct ratio with the phosphate of lime. We shall return to this subject in our remarks on "The Bones."

That a little phosphate of magnesia occurs in all the animal fluids and tissues is demonstrated by the analyses of the ash. The presence of this salt is very strikingly shown by a microscopic examination of the tissues of a dead body in which putrefaction has actively commenced: we observe that it is everywhere studded with the well-known crystals of the phosphate of ammonia and magnesia.

Phosphate of magnesia sometimes accumulates in large quantities in certain concretions; thus Brugnatelli[*] found a concretion in a human ovary consisting almost entirely of this earthy salt, and a similar one in the uterus, which was surrounded by a thin crust of phosphate of lime. A phlebolith, examined by Schlossberger[†] contained 58·7% of salts of lime, 13·7% of phosphate of magnesia, and 20·4% of organic matters.

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[*] Brugn. Giorn. T. 12, p. 164.

[†] Ann. d. Ch. u. Pharm. Bd. 69, S. 254.

The *origin* of the phosphate of magnesia is sufficiently obvious; for this salt occurs in all parts of plants, and particularly in the common varieties of grain that are used for food. From the ratio in which, as we have shown, the phosphate of magnesia stands to the phosphate of lime in the bones and other parts we may conclude that the animal economy requires far less of this salt than of the corresponding lime-salt; and this is especially illustrated by the fact that in different animals it is found that the intestinal canal absorbs all the phosphate of lime, but only very little phosphate of magnesia; for the excrements of the *carnivora*, as well as of the *herbivora*, contain an excess of the latter salt.

From these facts, Berzelius[*] long ago drew the conclusion that the absorbents of the intestinal canal have less tendency to take up phosphate of magnesia than phosphate of lime, but that rather more is always absorbed by the *herbivora* than by the *carnivora*; this latter fact, however, probably depends upon the circumstance that the food of the former contains far more magnesia than that of the latter class of animals. We should, however, be too strictly interpreting the meaning of Berzelius if we were to suppose that he considered the absorbents to possess any special power of selecting and taking up certain substances and rejecting others. The phenomenon in its whole extent is probably a mechanical one; the great tendency of the salts of magnesia to form crystals with the salts of the alkalies, may probably in some measure impede their free solution and resorption.

Berzelius found 12·9% of phosphate of magnesia, and 25·8% of phosphate of lime in the ash of the excrements, after the use of coarse bread and a little animal food. Fleitmann[†] found that, after the use, for some days, of a diet consisting of more animal than vegetable food, the excrements yielded an ash containing 10·67% of magnesia.

The common intestinal concretions of horses consist almost entirely of phosphate of magnesia and ammonia, with fragments of straw, &c.; in a concretion of this sort, Simon[‡] found 81% of phosphate of magnesia, but no salt of lime.

Physicians have paid much attention to the crystals of phosphate of magnesia and ammonia, which are very strikingly seen in typhous stools. Although these crystals are often enough to be found in the fæces in other diseases, it must be granted that their occurrence is by far the most frequently to be noticed in abdominal typhus; indeed, it is well known that the ulcerated patches of the intestine are usually thickly studded with minute crystals of this nature.

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[*] Lehrb. d. Ch. Bd. 9, S. 345.

[†] Pogg. Ann. Bd. 76, S. 383.

[‡] Buchner's Repertorium. Bd. 16, S. 215.

Phosphate of magnesia is always found in the urine of man and of carnivorous animals, and its presence is rendered very perceptible when the urine becomes alkaline, by the readiness with which it crystallises in combination with ammonia. As we shall return to this subject in the second volume, it is sufficient to observe in the present place, that these crystals are always formed in normal urine when alkaline fermentation commences. In serious lesions of the bladder or the spinal cord, we often find whole sediments consisting of these crystals. These deposits are, for the most part, either devoid of colour, or of a dirty white tint. In a specimen of diabetic urine, I once found a glistening white sediment, consisting entirely of these crystals, and not containing a trace of lime. Urinary calculi, consisting of pure phosphate of magnesia, are very rare, although more common than the *fusible* calculi which are composed of a mixture of phosphate of lime with phosphate of ammonia and magnesia.

FLUORIDE OF CALCIUM.

It is only in very minute quantities that this body occurs in the animal organism; it is, however, so integral a part of the enamel of the teeth, that we are inclined to ascribe to its presence (at least in part) the polish and the extraordinary hardness of that substance. The presence of small quantities of fluoride of calcium has been determined with certainty in the bones of almost all animals. More fluoride of calcium has been found in the skeletons of fossil animals than in those of our own time; and it is worthy of notice, that human bones found at Pompeii, contain, according to Liebig,[*] more fluoride of calcium that recent human bones.

Berzelius[†] found 2·1% of fluoride of calcium in the dentine and 3·2% in the enamel of a man's tooth, while the dentine and the enamel of that of an ox contained respectively 5·69% and 4% of this constituent. Marchand[‡] found 1% in the femur of a man aged 30 years, and Heintz[§], 2·05%.

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[*] Organ. Ch. auf Agricultur u. Physiol. angewendet, 1840, S. 140.

[†] Alt. Gehlen's Journ. Bd. 3, S. 1.

[‡] Journ. f. pr. Ch. Bd. 27, S. 83.

[§] Ber. d. Ak. d. Wiss. z. Berlin. Febr. 1849, S. 51.

Both Middleton[*] and von Bibra[†] have very carefully analysed the bones of various classes of animals, and have recognised the presence of fluoride of calcium not only in the bones of the mammalia, but also in those of birds, fishes, and reptiles, and even in the shells of the mollusca. Middleton's assertion that the bones of a 6½ months' fœtus contain as much fluoride of calcium as those of an adult, must be regarded as doubtful, till confirmed by further experiments.

Fluoride of calcium was first discovered in fossil ivory by Morichini[‡]; it has since been found in all fossil bones by Proust[§], Fourcroy and Vauquelin[||], Chevreul[¶], Brandes[**], Bergemann[††], Marchand, von Bibra, Middleton, and others. Lassaigne[‡‡] found as much as 15$\frac{0}{0}$ in the teeth of an Anoplotherium, and I[§§] found 16$\frac{0}{0}$ in the outer portion of one of the ribs of the Hydrarchos.

[The presence of fluorine in blood and milk has been clearly demonstrated by Dr. George Wilson[||||]. G. E. D.]

In regard to the origin of the fluoride of calcium we cannot doubt that the small quantities found in the animal body may be easily conveyed into the system with the food; we need only remember that many mineral waters contain traces of fluorides, and that plants take up a little fluoride of calcium from micaceous soils.

Fluoride of calcium was detected by Berzelius in the Carlsbad water, and has been found in other mineral waters; moreover, artificially prepared fluoride of calcium is by no means perfectly insoluble in distilled water. [According to Wilson 16 fluid ounces, or 7000 grains of water at 60° F, dissolve 0·26 of a grain of fluor spar. G. E. D.]

Whether the large quantities of fluoride of calcium which have been found in fossil bones are solely due to infiltration from without, must remain for the present undecided.

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[*] Philos. Mag. T. 25, p. 14.

[†] Op. cit.

[‡] A. Gehl. J. Bd. 3, S. 625; N. Gehl. J. Bd. 2, S. 177.

[§] N. Gehl. J. Bd. 2. S. 187.

[||] Ann. d. Chim. T. 57, p. 37.

[¶] Ibid. p. 45.

[**] Schweigg. Journ. Bd. 32, S. 505.

[††] Ibid. Bd. 52, S. 145.

[‡‡] Journ. de Pharm. T. 7, p. 1.

[§§] Carus, über den Hydrarchos. Dresd. 1846.

[||||] Edin. New Phil. Journ. Oct. 1850.

SILICA.

As the skeleton of the vertebrate animals chiefly owes its hardness to the phosphate of lime which it contains, and the shell of the invertebrate animals to the carbonate of lime, so the shields of the lowest classes of animals are rendered hard and firm by containing a large quantity of silica. This substance is so thickly deposited in these organs that neither decomposition nor incineration can destroy their form; hence it is that deposits of fossil infusoria are so often discovered.

Silica for the most part occurs only as an incidental constituent of the juices and tissues of the higher classes of animals; Gorup-Besanez* has, however, shown by numerous experiments that this body forms an integral constituent of *feathers* and of *hair*.

Small quantities of silica have also been found in the blood, in the white of egg, in the bile, in urine, and in the solid excrements, and occasionally in certain morbid concretions.

The *Bacillariæ* are the most remarkable of all the infusoria in relation to the quantity of silica which they contain; their shields equally resist the action of fire and of acids. We are indebted to Ehrenberg† for our first accurate knowledge on this subject, and for the discovery of fossil infusoria in flint, mountain meal, &c.

Henneberg,‡ as well as Gorup-Besanez, has determined the quantity of silica in feathers; the latter, however, has fully investigated the subject in all its bearings, and extends his enquiry to the determination of the influence exercised by species, age, food, and other circumstances on the deposition of silica in the feathers.

Gorup generally found from 0·11 to 2·47% of silica in the feathers of different birds, and from 6·9 to 65·0% of silica in the ash. The last-named quantity, which was the largest he ever found, occurred in the feathers of *Perdix cinerea*, but the feathers of *Strix flammea*, *Gallus domesticus*, and *Corvus frugilegus*, yielded ashes very rich in silica. The feathers of granivorous birds contained from 1·69 to 3·71% of silica (and their ash yielded from 25·5 to 50%); the feathers of birds living on fish and aquatic plants contained on an average 0·23%, and their ash 10·5% of silica; those of birds living on flesh and insects yielded, as a mean, 0·64%, and their ash 27%; and those of birds living on insects and berries 0·75%, and their ash 27%. Gorup usually found about twice as much silica in the feathers of old animals as in those of the young of the same species.

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* Ann. d. Ch. u. Pharm. Bd. 66, S. 321-342.

† Die Infusionsthierchen u. s. w. S. 143-169.

‡ Ann. d. Ch. u. Pharm. Bd. 61, S. 255-61.

In newly grown or young feathers only traces of silica were often to be found. In the pinions of the first order there was twice as much silica as in the tail-feathers of the second order; and in the tail and breast-feathers there was little more than in the pinions of the second order.

Berzelius found no silica in the *bones* or *teeth* of man; Fourcroy and Vauquelin[*] have, however, found it in the bones of children, and Marchand[†] in those of *Squalus cornubicus*; it has also frequently been found in fossil bones.

Silica has been found by Chevreul[‡] in sheep's wool, and by Vauquelin[§], and more recently by Laër[‖], in the human hair. Gorup has entered very fully into this part of the enquiry regarding the occurrence of silica. In brown human hair he found 0·22% of silica, the ash yielding 13·89%, while in the hair and wool of various animals he found sometimes rather more and sometimes rather less of this substance. The quantity of silica in the hair appears to be altogether independent of the nature of the food.

As silica occurs so constantly in the animal organism, it might naturally be expected that we should find it in the *blood*, and especially in that of birds. Millon[¶] found it in human blood; Weber[**] found that it amounted to 0·19%, in the ash of ox-blood, and in hens' blood Henneberg[††] found 0·96%.

Poleck[‡‡] found 7·05% in the ash of the *white of egg*; silica has also been found in the *bile*, *urine*, and *solid excrements*. Weidenbusch[§§] found 0·36% in the ash of ox-bile; Pleisch[‖‖] and Bley[¶¶] detected it in gall-stones, and Mitscherlich[***] found a trace of it in the saliva. Berzelius[†††] was the first who discovered traces of it in human urine; Fleitmann* has since found it in the ash of the urine, and Fourcroy and Vauquelin†, as well as de Koninck and Wurzer‡ in urinary calculi. It need cause no wonder that silica is often found in the contents of the intestines, as it is widely distributed throughout the vegetable kingdom.

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[*] Ann. de Chim. T. 72, p. 282.

[†] Lehrb. d. phys. Ch. S. 97.

[‡] Compt. rend. T. 10, p. 632.

[§] Ann. de Chim. T. 58, p. 41.

[‖] Ann. d. Ch. u. Pharm. Bd. 44, S. 172.

[¶] Journ. de Pharm. 3 Sér. T. 13, pp. 86-88.

[**] Pogg. Ann. Bd. 76, S. 387.

[††] Op. cit.

[‡‡] Pogg. Ann. Bd. 76, S. 360

[§§] Ibid. S. 369.

[‖‖] Kastn. Arch. Bd. 8, S. 300.

[¶¶] Journ. f. pr. Ch. Bd. 1, S. 115.

[***] Pogg. Ann. Bd. 26, S. 320.

[†††] Lehrb. d. Chem. Bd. 9, S. 433.

That the quantity of silica occurring in the animal organism essentially depends on the greater or lesser quantity of silica in the food, and consequently, that the origin of this body must be principally referred to vegetable food and siliceous water (and further, perhaps, in the case of birds, to the sand which they swallow,) is rendered sufficiently evident from the experiments of Gorup-Besanez, if, indeed, any demonstration of the fact were required.

Plants contain far more silica than was formerly supposed; in the *Equisetaceæ*, for instance, the ash often contains 97%. The best method of exhibiting its presence in the seeds of the grasses, is by moistening them with a little nitric acid before incinerating them; in this manner, and with the aid of the microscope we may, according to Schultz, recognise the presence of this substance, not only in the husks but also in the ovaries of many of the monocotyledons. Hence, it is obvious, that we must receive silica into the system with the bread; we can thus readily understand how it was that, after the use of rye-bread, Berzelius§ found 1·016% in the solid excrements, and why it is that the dung of the *herbivora*, (whose food consists of those parts of plants which are richest in silica,) contains so large a quantity of this substance. In the dung of the cow, Zierl‖ found 4·4%, in that of the sheep, 6·0%, and in that of the horse, 4·6%. Hence, large quantities of silica are often found in the intestinal concretions of herbivorous animals.

SECOND CLASS OF MINERAL BODIES.

HYDROCHLORIC ACID.

As we are convinced by the reasons given in p. 93, that lactic acid is the essential free acid of the gastric juice, we need devote no special consideration to this acid. It is sufficient to remind our readers, that, according to our experiments,* lactic acid can be replaced by no other acid, except hydrochloric acid, in the process of digestion.

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* Pogg. Ann. Bd. 76, S. 358.

† Syst. des Connoiss. Chim. T. 10.

‡ Schweig. Journ. Bd. 36, S. 321.

§ Lehrb. d. Chem. Bd. 9, S. 346.

‖ Kastn. Arch. Bd. 2, S. 476.

HYDROFLUORIC ACID.

Brugnatelli† believed that he had discovered the existence of this acid in the gastric juice of birds, when he found that pieces of agate and rock-crystal, which he introduced by means of tubes into the stomachs of common fowls and turkeys, were distinctly corroded, and had lost from 12 to 14 grains in weight, on their removal after ten days; and Treviranus‡ also believed that, when the contents of the intestinal canal of fowls were digested in porcelain vessels, the glazing was attacked.

In reference to the small quantities of this acid which might possibly occur in the gastric and intestinal juices of these animals, it is certainly difficult to demonstrate its absence in an unquestionable manner; but as theoretical reasons as well as direct experiments are opposed to Brugnatelli's view, we may, at all events, with great probability, assume the non-occurrence of this acid. Tiedemann and Gmelin,§ digested the gastric juice of a duck for 24 hours in a platinum crucible, which was covered with a piece of glass having a coating of wax through which a few lines were drawn; they could, however, detect no corrosion on the glass. I placed the chyle of a duck which had just been killed, in a platinum crucible, treated the mass with a little sulphuric acid, and covered the crucible with a watch-glass coated with wax except at the centre (the inferior convex part) where its surface was bare and exposed; at the termination of the experiment, I could not find the slightest corrosion on the watch-glass. Further, I saturated with potash the fluid obtained by washing the contents of the crop and stomach of two turkeys with water, evaporated it to dryness and burned the residue; the ash was then carefully treated with sulphuric acid in a platinum crucible, in the manner already described, but here also no trace of hydrofluoric acid was obtained.

If these experiments are not sufficiently stringent to overthrow the observations of Brugnatelli, they at all events serve to explain how it was that Brugnatelli and Treviranus were led to adopt this view. For it is very possible that, as we always find small pebbles and sand in the stomachs of these animals, a purely mechanical attrition of the finest granules of sand may have apparently corroded the pieces of agate and rock-crystal during their long sojourn in the stomach, and thus have occasioned their loss of weight. Moreover, I have never been able to detect any decided corrosion of the pebbles which we find in the stomachs of ducks and fowls. It would be strange if nature had here first ordained the secretion of hydrofluoric acid, in order that it should immediately again disappear through the action of the siliceous pebbles which are swallowed by birds. Should not the hydrofluoric acid, if it were present, expel other acids from the salts contained in the gastric juice?

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* Ber. d. k. sächs. Ges. d. Wiss. z. Leipzig. 1849.

† Crell's Ann. 1787. Bd. 1, S. 230.

‡ Biologie. Bd. 4, S. 362.

§ Verdauung. Bd. 2, S. 139.

Chloride of Sodium.

In almost every portion of the earth's surface we find this body in all parts of the animal organism; and it is not a mere incidental constituent conveyed into the system with the food and drink, but it is applied to definite, although highly various ends.

The importance of chloride of sodium in the metamorphosis of the animal tissues is illustrated by the fact that it always forms the greatest part of the soluble constituents of the ash of all animal substances. It is very constantly associated with certain animal matters, and essentially influences their chemical and physical properties; thus albumen in part owes its solubility to the chloride of sodium contained in it, and the differences which it presents in coagulating are in part dependent on the quantity of this salt that is present. Chloride of sodium dissolves pure casein, and has a singular power of impeding the coagulation of the fibrin of the blood. If it is impossible to prove that chloride of sodium forms definite chemical compounds with these bodies, the following considerations at all events render such a view probable;—namely, the influence this salt exercises on the above named protein-compounds, the analogy of the compound of chloride of sodium and glucose, and finally the impossibility, by mere washing, of perfectly separating some of the protein-compounds from the chloride of sodium.

We would especially refer the reader to the relation of albumen towards salts, described in p. 332.

In accordance with these facts we find that the chloride of sodium, like other important constituents of the animal body, is not merely constantly present, but also that it is combined in tolerably definite proportions in the different constituent parts. For it is an established law, that the different animal fluids always strive to attain a similar chemical constitution. This law, to which we must subsequently recur more in detail, includes the protein-compounds, which, if they are taken in excess, certainly are decomposed in the ordinary manner, but are eliminated as rapidly as possible by the kidneys under the form of urea and uric acid.

The chloride of sodium in normal human blood stands in a tolerably constant ratio to its other soluble constituents, the limiting ratios being 3 : 1 and 2·4 : 1. Berzelius* found 6 parts in 1000 of the serum of human blood, and Marcet† 6·6 in 1000 parts of blood, which corresponds to about 5·5 in 1000 of serum; Nasse‡ obtained from 4 to 5 parts of chloride of sodium from 1000 of blood, Denis§ from 3·537 to 3·668 parts, and Becquerel and Rodier|| from 2·3 to 4·2 parts; the mean of 11 analyses of men's blood yielding 3·1, and of 8 analyses of women's blood 3·5 parts. In 1000 parts of my own blood in a normal state I found 4·138 parts of chloride of sodium, and after the use of very salt food, which caused intense thirst, it amounted to 4·148; an hour after taking two ounces of salt, and having in the interval drank about two quarts of water, the quantity was 4·181. Hence it seems to follow that the animal organism not only removes foreign substances with extraordinary rapidity, but that even useful substances, if they are in excess, are as rapidly as possible eliminated.

The amount of salt in the blood undergoes great fluctuations in different diseases; thus Nasse¶ and Scherer** found that there was a diminution of the chloride of sodium in inflammatory blood; O'Shaugnessy, Rayer, and Mulder observed this strikingly in cholera; Nasse also observed it in the blood of a diabetic patient, Lecanu in cases of jaundice, and Jennings and Simon in chlorotic patients: an augmentation of the salt in the blood has been noticed by Fremy in sea-scurvy and by Nasse in the rot in sheep. My experiments have left it very doubtful whether the salts of the blood are diminished in tuberculosis, since it is not often that we can obtain the blood of tuberculous patients, except when some inflammatory attack gives occasion for the abstraction of blood. We shall return to this subject more fully in the second volume, when considering "The Blood."

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* Lehrb. d. Chem. Bd. 9, S. 98.
† Medico-Chir. Trans. Vol. 2, p. 370.
‡ Handwörterbuch d. Physiol. Bd. 1, S. 167.
§ Journ. de Chim. méd. T. 4, p. 111.
|| Gaz. méd. 1844, No. 48.
¶ Das Blut. 1836, S. 287.
** Haeser's Arch. Bd. 10.

Even if the well known action of chloride of sodium on the colour of the blood be entirely dependent on mechanical relations, the occurrence of almost constant quantities of this salt in the blood during health, and its considerable variations in different diseases, and, further, its chemical action on histogenetic substances, indicate that in all probability it takes some definite chemical part in the metamorphosis of the blood. Hofmann* believes that it increases the capacity of the constituents of the blood for oxidation, which however, requires proof.

Berzelius was formerly of opinion that the quantity of albumen contained in the serum of the blood might be the cause why the blood-pigment which is so readily soluble in pure water did not dissolve in the serum, but Joh. Müller has shown that the capsules of the blood-corpuscles dissolve, if they are brought in contact with an aqueous and not too dilute solution of albumen; if, however, we treat the albumen with a little water containing only 1% of chloride of sodium, the corpuscles remain unchanged, whereas they are destroyed by a pure solution of salt containing no albumen.

We shall treat, at some length, of the mode of action of chloride of sodium and various other bodies on the red colour of the blood, in the second volume. It is here sufficient to remark that Scherer's experiments have clearly demonstrated that the bright or dark colour of the blood principally depends on the form of the blood-corpuscles, which again is chiefly dependent on the endosmotic relations existing between their contents and the surrounding fluid. For instance, if we add much salt to blood, the corpuscles become contracted and biconcave; it is to this biconcave form that Scherer attributes the brighter colour of the blood.

In those fluids which are secreted from the blood and which contain a larger quantity of chloride of sodium than the blood itself, as, for instance, the saliva, gastric juice, inflammatory exudations, pus, and mucus, this salt doubtless discharges some important functions. We claim no high importance for it in the saliva; but if that fluid exercises a function, the chloride of sodium certainly takes part therein, since its quantity exceeds that of all he other constituents of the saliva. In the gastric juice we find, in addition to a little organic matter, scarcely anything but metallic chlorides, and chiefly chloride of sodium.

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* Das Protëin u. s. w. S. 19.

From the abundance in which it exists both in the saliva and the gastric juice we miget be led to infer that it essentially promotes the solution of the food, and its future changes, or at all events, that it contributes to impede abnormal decompositions and metamorphoses of the food.

Several observations which I have made, tend to show that the excess of salt conveyed into the blood is not merely carried off by the kidneys with the greatest possible rapidity, but also by other secreting organs, as the salivary glands, the gastric glands, &c. While the gastric mucous membrane of a dog with a fistulous opening into the stomach, secreted a juice, when the stomach was empty and artificially stimulated, which, according to Blondlot, contained 0·126% of chloride of sodium, I obtained a gastric juice in a similar manner from a dog into whose jugular vein I had half an hour previously injected two ounces of a saturated solution of salt, which contained 0·385%. These facts are rendered more perceptible by using either of the analogous salts, the iodide of sodium or of potassium; iodide of potassium, when injected into the veins, appears with extreme rapidity in the stomach, although I am not quite certain whether this is not in a great measure dependent on its very rapid presence in the saliva, and on its finding its way into the stomach through that fluid; for I have convinced myself that the iodide of potassium passes from the blood in larger quantity, and with more rapidity, into the saliva than into the urine. If we take a few grains of iodide of potassium in the form of pills, and at once convince ourselves that no iodine is retained in the buccal fluids, we can in the course of from 5 to 10 minutes recognise iodine with certainty in the saliva, although it cannot be then detected in the urine even if we examine that fluid directly after its secretion by the kidneys, as it drops from the ureters. Bernard* has made similar observations with prussiate of potash, lactic acid, and other substances; after injection into the jugular veins of a dog, they very rapidly appeared in the gastric juice.

Enderlin† found 61·93% of the chlorides of sodium and potassium in 100 parts of the mineral constituents of saliva.

Prout‡ found from 0·12% to 0·13% of the chloride of sodium with a little chloride of potassium in human gastric juice; Braconnot§,

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* Thèse soutenue à la faculté de Paris, 1844.

† Ann. d. Ch. u. Pharm. Bd. 50, S. 56.

‡ Phil. Trans. for 1824, p. 45.

§ Ann. de Chim. et de Phys. T. 59, p. 113.

Tiedemann and Gmelin*, and Berzelius agree in stating that the gastric juice is rich in this salt. I found 0·311% of chloride of sodium in the fluid from the crop of a duck which for eight days had been only fed with barley moistened with distilled water.

That the chloride of sodium, and the metallic chlorides generally, which are contained in the gastric juice, contribute at all to the solution of the histogenetic substances is not probable; for, notwithstanding some of my earlier experiments which seemed to support that view, more recent and more numerous experiments† have convinced me that any addition of salt, either to natural or well prepared artificial gastric juice, infallibly retards the changes which the articles of nitrogenous food undergo. We may presume that a definite quantity of the metallic chlorides exists in some form of chemical combination in the gastric juice; this quantity being exactly sufficient to hinder any abnormal decomposition in that fluid, without checking its digestive power.

In the exudations we certainly find less chloride of sodium than in the blood itself, but in relation to the fixed constituents of these liquids, this salt is always considerably increased. The investigations of Brücke‡ and Henle§ have proved, almost beyond a doubt, that this abundant transudation of soluble salts through the walls of the vessels is dependent on a purely mechanical relation. It is, however, not improbable that the chloride of sodium coöperates in the metamorphosis of the exudation; we find, at least, that pus and other exudations in which cells become developed, are very rich in this salt; and this is especially the case with mucus, as has been shown by Nasse‖. The fluid of cancerous growths always contains a large quantity of this salt. Whether the chloride of sodium takes part in the abnormal conversion of the exudation into cells, is a question that must be at present left undecided. We are almost led to the belief that every deposition of cells is accompanied by an increase in the quantity of chloride of sodium, or that this salt arrests their development at a low stage. We find at least that the cartilages, which, in their perfectly developed state abound in cells, contain far more chloride of sodium than occurs in other parts of the animal body. The cartilaginous bones of the fœtus, before much phosphate of lime has been deposited, contain far more chloride of sodium than adult bones: and abnormal depositions of bony matter contain more of this salt than even the permanent cartilages.

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* Verdauung. Bd. 1, S. 91.

† Ber. d. k. sächs. Ges. d. Wiss. 1849.

‡ Casper's Wochensch. 1840, No. 21.

§ Zeitschr. f. rat. Med. Bd. 1, S. 122.

‖ Journ. f. prakt. Ch. Bd. 29, S. 59.

Fromherz and Gugert* found 8·231% of chloride of sodium in the ash of the costal cartilages of a man aged 20 years; I found 11·236% of this salt in the ash of the laryngeal cartilages of an adult female. From various bones I could only extract from 0·7 to 1·5%. The femur of a six-months' fœtus which I examined contained 10·138% of chloride of sodium, and according to Valentin† the encrusting exudation, deposited around a carious tibia, contained 13·7%.

Nasse, taking the mean of two analyses, found that the chloride of sodium in the mucus of the air-passages amounted to 0·582%, while two comparative analyses showed that it amounted to 0·46% in the serum of the blood, and to 1·26% in that of pus. Hence in this respect pus approximates closely to mucus, while the serous portions of blood and pus are differently constituted.

In order to give a general view regarding the occurrence of chloride of sodium in the animal fluids, I append the following table, which is based, in a great measure, on my own analyses; *a* signifies the amount of salt in 100 parts of the fluid, *b* in 100 parts of solid residue, and *c* in 100 parts of ash.

	a.	*b.*	*c.*
Human blood	0·421%	1·931%	57·641%
Blood of the horse	0·510%	2·750%	67·105%
Chyle	0·531%	8·313%	67·884%
Lymph (Nasse)	0·412%	8·246%	72·902%
Serum of the blood (Nasse)	0·405%	5·200%	59·090%
Blood of the cat (Nasse)	0·537%	2·826%	67·128%
Chyle (Nasse)	0·710%	7·529%	62·286%
Human milk	0·087%	0·726%	33·089%
Saliva	0·153%	12·988%	62·195%
Gastric juice of the dog	0·126%	12·753%	42·089%
Human bile	0·364%	3·353%	30·464%
Urine	0·332%	5·187%	22·972%
Mucus (Nasse)	0·583%	13·100%	70·000%
Serum of the blood (Nasse)	0·460%	4·919%	58·974%
Serum of pus (Nasse)	1·260%	11·454%	72·330%
Inflammatory exudation in the pleura (Scherer)	0·750%	10·416%	73·529%
Scirrhus of the breast	0·314%	6·043%	65·391%

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* Schweigg. Journ. Bd. 50, S. 187.

† Repertor. 1838, S. 301.

After this general view of the occurrence and uses of salt in the animal economy, it is hardly requisite to allude to the sources from which the animal body receives its due supply. Chloride of sodium is so generally distributed throughout nature, that this necessary quantity is conveyed into the organism with the ordinary food and with the water.

The habits of civilized life have elevated salt to the rank of a positive necessary, but we must by no means conclude from this circumstance that the salt contained in ordinary food is not sufficient for the support of the animal functions. A simple comparison of the quantity of salt contained in the animal body, with that which we are daily taking with the food, at once shows that we use more salt than is requisite: and if, on the one hand, as several travellers narrate, certain negro tribes in the interior of Africa exchange gold-dust for an equal weight of salt, and in want of it have recourse to the most disgusting substitutes; we know, on the other hand, that whole races in the South Sea Islands, and in South America, flourish without even the knowledge of this substance. Further, as Liebig has shown, tempests carry salt from the ocean far into the interior, and thus supply the spring water with it. A glance at the results of the analyses of the ashes of plants, is sufficient to show that the ordinary articles of vegetable food are perfectly sufficient to supply the necessary quantity of salt to the animal body.

CARBONATE OF SODA.

This salt not unfrequently occurs in the ash of burned animal matters, but in most cases it is merely the product of the combustion of combinations of soda with organic acids or protein-compounds. Investigations deserving of the greatest confidence prove however that carbonate of soda, together with other soda-compounds, exists in the blood and in the lymph. It is also contained, together with large quantities of the carbonate of potash and lime, in the urine of herbivorous animals.

The earlier observers assumed the presence of carbonate of soda in the blood as a recognised fact; and indeed it was believed to take an active part in the excretion of carbonic acid; but certain later investigations seemed to leave it very doubtful whether alkaline carbonates exist in the blood. Alkaline carbonates were always found in the ash of blood, (as for instance, by Berzelius, Marcet, Mitscherlich, Tiedemann and Gmelin, and more recently by Nasse, Marchand, and others,) till Enderlin[*] announced that blood incinerated according to his method, left an ash which did not yield a trace of carbonic acid. He examined the ash of the blood of men, oxen, sheep, and hares, and found that in addition to the ordinary chlorides and sulphates, the soluble salts consisted solely of tribasic phosphate of soda. Hence he concludes that as no carbonates can be found in the ash, it is altogether impossible that any carbonated alkali can occur in the blood. But it does not follow that the earlier observers were in error, when they found carbonate of soda in the blood, (Nasse[†], for instance, found from 0·06 to 0·08%, and Marchand[‡], 0·125%,) for we can at pleasure prepare a blood-ash either with or without carbonates, according to the degree of heat and the method of incineration we employ. If we heat common phosphate of soda ($2NaO . HO . PO_5$) with carbonate of soda, the latter loses its carbonic acid, and as a necessary consequence there is formed the tribasic phosphate of soda; when dissolved in water, this tribasic phosphate of soda very rapidly absorbs carbonic acid from the atmosphere, and becomes converted into carbonate and *c* (common) phosphate of soda. Hence tribasic phosphate of soda cannot exist in the circulating blood, since this fluid contains sufficient carbonic acid to ensure its decomposition.

Assuming that carbonate of soda exists in the blood-ash, this by no means proves that it is present in fresh blood, for this fluid contains fatty and other organic acids in combination with alkalies, which on incineration are converted into carbonates. But if we consider that fresh blood always has an alkaline reaction, and that, in consequence of its always containing carbonic acid, caustic soda can no more occur in it than the above-mentioned tribasic phosphate of soda, this reaction can hardly be attributed to any other body than to carbonate of soda; for the combinations of the fatty acids with alkalies are contained in the blood in far too small quantities to account for the alkaline reaction of that fluid, and the amount of carbonate present in the ash. Liebig[§] was the first to remark that the carbonate of soda must be contained in the blood as a bicarbonate. No free acid can be present with common carbonate of soda. The following experiment favours the view of the presence of the bicarbonate: if we precipitate the serum of the blood with alcohol and thoroughly wash the precipitate with dilute spirit, the albumen on incineration leaves no alkaline ash; if soda were chemically combined with albumen, the soda must be precipitated with the albumen, while neutral carbonate of soda and especially the bicarbonate dissolve readily in spirit. On passing hydrogen through the fluid from which the albumen has been removed by filtration, carbonic acid is expelled; for as Magnus and Rose formerly proved, and as Marchand[*] has recently again demonstrated, hydrogen completely expels the one atom of carbonic acid from the bicarbonate of soda, especially if the temperature be raised to 38°. Liebig also adduces the relation of corrosive sublimate to the fluid freed from the albumen by spirit of wine, in evidence of the presence of bicarbonate of soda; for, on the addition of corrosive sublimate to this fluid, there is no precipitate, but after some time there are deposited brown crystals of oxychloride of mercury, precisely as would have occurred if this reagent had been added to a solution of bicarbonate of soda. By means of a current of pure hydrogen gas, and by the repeated application of the air-pump, I so thoroughly removed the carbonic acid from freshly whipped ox-blood, that a fresh stream of hydrogen passed through the blood no longer produced the slightest turbidity in baryta-water; by means of a special contrivance, so as to exclude the access of the air, a little acetic acid was forced into the blood by means of the hydrogen gas, and the latter was again passed in considerable quantity through the blood; immediately after the addition of the acetic acid to the blood the baryta-water was rendered turbid by the current of hydrogen. We thus obtain a proof that a certain quantity of the carbonic acid in the blood exists in combination with a base, in addition to that which can be expelled by gases and extracted by the air-pump. Hence there can no longer be any doubt regarding the presence of carbonate of soda in the blood. I have found, taking the mean of ten carefully conducted quantitative analyses,[†] that ox-blood contains 0·1628% of ordinary carbonate of soda, after the expulsion of the free carbonic acid in the manner which has already been described.

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[*] Ann. d. Ch. u. Pharm. Bd. 50, S. 53.

[†] Handwörterb. der Physiolog. Bd. 1, S. 167.

[‡] Lehrb. d. physiol. Chem. S. 226.

[§] Handwörterb. der Chem. Bd. 1, S. 901.

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[*] Journ. f. pr. Chem. Bd. 35. S. 390.

[†] Ber. d. k. sächs. Ges. d. Wiss. 1847, S. 96-100.

Nasse* found 0·056% of carbonate of soda in the lymph of a horse, while Marcet† found 0·165% in the serum of the blood. Those who regard the kidneys as mere percolators cannot deny the presence of alkaline carbonates in the blood, since the urine (at least of herbivorous animals) contains a considerable amount of carbonates. The parotid saliva of the horse becomes turbid, in the same manner as lime-water, on exposure to the air, with, however, this difference, that it almost immediately deposites the most beautiful microscopic crystals of carbonate of lime.

Liebig was formerly of opinion that the carbonate of soda in the blood acted an extremely important part in the process of respiration, in short, that it was the means by which the carbonic acid is conveyed from the capillaries into the lungs. The oxygen mixed with the blood in the lungs there displaces the carbonic acid as completely as it would be expelled by a current of oxygen or hydrogen from its state of combination in bicarbonate of soda. As far as our present knowledge extends, no facts are at variance with this view; indeed, if the presence of carbonate of soda in the blood be once granted, no one can wonder that it is converted to the bicarbonate, and on the other hand, that it must be decomposed on coming in contact with other gases than carbonic acid. But the question naturally suggests itself—Is the quantity of carbonate of soda sufficient to serve as a means of transport for the whole of the carbonic acid of the blood? The following calculation supplies the answer: 1000 grammes of blood contain 1·628 grammes of carbonate of soda, which, to become converted into bicarbonate must take up 0·637 of a gramme of carbonic acid; hence 0·637 of a gramme of carbonic acid can be extracted from the blood by the air-pump, or expelled by other gases; this would amount to 322 cc. according to volume; if we assume that the specific gravity of the blood is 1·055, then 1000 cc. of blood would contain 343 cc. of carbonic acid, capable of being removed by other gases or by the air-pump. Magnus has, however, succeeded in removing about 300 cc. of carbonic acid from 1000 cc. of blood by means of hydrogen and a vacuum; a method by which a part of the carbonic acid must always remain in the blood. The coincidence between the empirical result and the calculation is quite as great as could be expected.

It cannot be doubted that the carbonate of soda in the blood serves as a solvent for the fibrin as well as the albumen; Bird, has, however, shown that the bicarbonate is one of the best solvents for albumen. It is well known that large quantities of the alkaline carbonates have the property of impeding or altogether preventing the coagulation of the fibrin.

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* Simon's Beiträge z. phys. u. pathol. Chem. Bd. 1, S. 449.

† Medico. Chir. Trans. vol. 2, p. 370.

Finally, that the alkali of the blood also contributes to saturate the acids conveyed into the organism or formed within it, is the more probable, because nature seems to have provided that the alkaline carbonates shall be produced as rapidly as possible from the combinations of potash and soda with vegetable acids. (See p. 97.)

The origin of carbonate of soda in the animal body is so obvious, from the preceding observations, that it is unnecessary to enter further into the subject.

ALKALINE PHOSPHATES.

Important as the alkaline phosphates doubtless are in the metamorphosis of animal tissue, we are unable at present to state much with certainty regarding them. Before Rose had introduced his new method of preparing and analysing the ashes of organic bodies, it must have been concluded from the abundant occurrence of alkaline phosphates in the ashes of animal substances, that these salts played an important part in the animal economy. This conclusion seemed especially to be supported by the peculiar relations of the saturating capacity of phosphoric acid, and by the metamerism of the phosphates. For it is almost self-evident that no salts of any other acid could be so usefully applied in the metamorphosis of tissue, as those of phosphoric acid, which can form neutral salts with one, two, and three atoms of base, acid salts with one and two atoms, and likewise several basic salts. Moreover it must be recollected that common phosphate of soda may contain one atom of basic water in place of one atom of fixed base, and thus by its alkalinity it may serve, like free alkalies or their carbonates, as a solvent for many animal substances;—that it has the property of yielding to the weakest acids, as, for instance, uric acid, one of the two atoms of fixed base, and of being converted into an acid phosphate;—and finally, that the ordinary basic phosphate of soda (with 3 atoms of fixed base) yields 1 atom of soda to free carbonic acid, and thus gives rise to two neutral salts both of which, however, have an alkaline reaction, and a strong solvent *power.*

Taking all these circumstances into consideration, and moreover recollecting the importance of the earthy phosphates, and especially of the animal substances containing phosphorus, we might be disposed to believe the conclusion justified, which, it was supposed, might be drawn from the abundance with which alkaline phosphates occur in the ash. But, unfortunately, Rose's improved analyses of the mineral constituents occurring in animal bodies have deprived us of the basis on which this conclusion rests. The earlier ash-analyses of the different animal juices can no longer be regarded as affording evidence of the importance of these alkaline phosphates: later and more perfect analyses, in accordance with Rose's method, do not enable us to form a decided opinion regarding the occurrence of preformed alkaline phosphates in the different animal fluids, for it is not only the alkaline phosphates contained in the aqueous extract of the carbonaceous residue of animal bodies which are to be regarded as preformed in the animal body, but also those contained in the hydrochloric extract, which were retained in the residue with phosphate of lime or of magnesia as insoluble double salts (Rose*).

We cannot decide, in reference to these alkaline phosphates, whether previously to their combining with lime or magnesia, they existed preformed as basic alkaline phosphates, or rather, as Rose thinks more probable, as alkaline carbonates or combinations of alkalies with organic acids; further, it has never been quite accurately determined to what extent alkaline phosphates are produced from phosphate of magnesia when decomposed by alkaline carbonates. But putting out of view all these uncertainties, we should not be too hasty in drawing conclusions from the results of such analyses of the mineral constituents; for the principle asserted by Rose that the mineral bodies which cannot be extracted by hydrochloric acid from the carbonaceous residue of animal substances must be regarded as non-oxidised, and as combinations of phosphuretted radicals with metals, is at present only an hypothesis, although a very probable one. Such are the reasons which determine us for the present to suppress any consideration of the part which the alkaline phosphates may take in the general metamorphosis of matter, or in individual animal processes. If however, further investigations demonstrate, with greater certainty, the more abundant occurrence of these phosphates in the individual animal juices and in certain processes, our knowledge of the properties of phosphate of soda, would readily lead us to understand in what manner the alkaline phosphates would act in the different processes.

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* Pogg. Ann. Bd. 77, S. 288-302.

In order to give some sort of general idea how, according to Rose's analyses, the preformed alkaline phosphates should stand in relation to the other mineral constituents, we have collected, in the following table, the results of the analyses of several animal substances, conducted under Rose's superintendence.

There are yielded by 100 parts of the ash of	Salts which can be extracted from the carbonaceous residue by water.	Alkaline phosphates contained in 100 parts of the soluble salts.	
Ox-blood	60·90	$3KO.PO_5$	1·58
Horse-flesh	42·81	$2NaO.PO_5$ $2KO.PO_5$	11·10 83·27
Cow's milk	34·17	$3KO.PO_5$	21·60
Yolk of egg	40·95	$KO.PO_5$ $NaO.PO_5$	24·57 25·16
White of egg	81·85		0·00
Ox-bile	90·85	$3KO.PO_5$ $3NaO{\cdot}PO_5$	6·78 14·51
Urine	90·87	$2KO.PO_5$ $3KO.PO_5$	16·12 4·55
Solid excrements	18·55	$3KO.PO_5$	20·13

Even these few numerical results promise to throw much light on the theory of the metamorphosis of animal substances, on the nature of individual zoo-chemical processes, on the distribution of the potash and the soda in the different animal fluids, on the physiological importance of phosphorus, &c. Notwithstanding the confidence which we are justified in placing on the accuracy of these analyses, we avoid entering deeply into the conclusions that might be deduced from them, for independently of the circumstance that so few analyses afford us comparatively little means of establishing theories and deductions, we shall find sufficient occasion, when considering the animal substances named in the above table, to revert to the *data* afforded by these experiments, especially as our observations would extend to too great a length, if we were to attempt to bring into unison, or to estimate as they deserve, the often contradictory results of the earlier analyses.

Thus, for instance, in the consideration of the muscular tissue and of the fluid with which it is saturated, we shall enter into the beautiful views which Liebig, with his customary skill, has developed in his classical memoir on this subject. He has there particularly directed attention to the different proportions in which potash and soda exist in the blood and in the muscular fluid; this very important difference is less marked in Rose's analyses of the mineral constituents of both fluids, and taking into consideration the importance of the subject, it is exceedingly necessary, in order that we should have a clear insight into these relations, that we should form a decisive opinion regarding the value of the facts in our possession.

A glance at the numerous analyses of the ashes of plants, and especially of their seeds, is sufficient to indicate the *source* of the phosphates in the animal body; the copious discharge of phosphates by the urine need scarcely excite our wonder, as it includes both those which were contained preformed in the food, and those which are formed during the metamorphosis of animal tissue, by the oxidation of the phosphuretted organic matters or radicals.

IRON.

This metal occurs in the animal body, not only in very different parts, but also in different conditions; in the blood, as we have already shown in our observations on hæmatin, it seems highly probable that it exists, for the most part, in a non-oxidised state; in the gastric juice it exists, according to Berzelius, as a protochloride, and in other fluids as a phosphate.

According to Rose's method, the ash of ox-blood contains 6·84% of peroxide of iron, that of horse-flesh 1·00%, that of milk 0·47%, that of the yolk of egg 1.85%, that of the white of egg 2·09%, that of the bile 0·23% and that of the fæces 2·09%. We have already noticed the presence of iron in black pigment in our remarks on melanin. Large quantities of iron are sometimes found in the ashes of gall-stones, especially of such as consist chiefly of pigment. There appears to be no relation between the colour of the hair, and the quality of the iron which it contains. (Laër.*)

We are unfortunately perfectly ignorant regarding the special uses of iron in the animal economy. In reference to the iron in the blood, we have already seen (p. 308) that it is in some way connected with the function of the corpuscles, but we know nothing further. But since the iron is of especial importance in the animal body, we cannot wonder at its occurrence in the milk and in the egg. If we find iron in the bile, its occurrence there is easily explained, if we adopt the view that this fluid is for the most part produced from the destruction of the blood-corpuscles.

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* Ann. d. Ch. u. Pharm. Bd. 45, S. 227.

The fluid and solid articles of food contain so much iron that a portion of it is always thrown off with the solid excrements. Nature has provided that the animal organism shall receive the necessary quantity of this essential metal with every kind of food.

THIRD CLASS OF MINERAL BODIES.

ALKALINE SULPHATES.

Sulphates occur in most of the animal fluids, with the exception of the urine, in extremely small quantities; and, indeed, in several, as, for instance, the milk, the bile, and the gastric juice, they are altogether absent. They are also contained in comparatively minute quantities in the blood. Hence it may be concluded that these salts are of no essential use in the animal organism; a view which is confirmed by the fact that as soon as they are taken into the body, they are as rapidly as possible eliminated either with the solid or the fluid excrements. On the other hand, it is worthy of remark, that v. Bibra* found considerable quantities of soda in the bones of reptiles and fishes.

Berzelius† and Simon‡ found no sulphates in the milk, and Braconnot§ and Berzelius‖ also failed to detect them both in the gastric juice, and in the bile of man and the ox.

If we treat the dry residue of the serum of the blood, milk, saliva, bile, &c., with spirit, till it ceases to extract anything additional on boiling, and if we then extract the insoluble residue with water, precipitate the aqueous solution with a little tannic acid, evaporate the filtered fluid, again extract with spirit, and dissolve the residue in water, the aqueous solution only seldom exhibits any traces of sulphates. That sulphate of soda is frequently found even in considerable quantity in the ash of these animal fluids, and indeed that it must be found there, is sufficiently explained by the remarks we have already made regarding the changes which the mineral constituents of animal substances undergo on incineration. The bile presents one of the best examples of these changes, for its ash is very rich in sulphates, while we can hardly discover a trace of them in the fresh fluid.

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* Chem. Unters. über die Knochen u. Zähne. S. 226 u. 242.

† Lehrb. der Chem. Bd. 9, S. 695.

‡ Frauenmilch. S. 43.

§ Op. cit.

‖ Jahresber. Bd. 16, S. 379.

The frequent use of the alkaline sulphates in medicine might almost lead to the presumption, that these salts when conveyed into the system with the food, are not devoid of use in relation to the physiological functions of the animal organism, and in particular to that of digestion. When on the one hand we take into consideration the changes which the alkaline sulphates undergo in the process of digestion, and, on the other, the occurrence of highly sulphuretted organic substances in the animal organism, great probability seems to attach to this view. The experience of physicians, and direct physiologico-chemical experiments have clearly proved, that small quantities of alkaline sulphates are converted in the intestinal canal during digestion into sulphides. Hence we might conclude that these salts take part in the production of such highly sulphuretted animal substances as taurocholic acid, horny tissue, &c., but as substances which contain sulphur, such as legumin, gluten, &c., enter the animal body with the vegetable food, these highly sulphuretted substances, peculiar to the animal body, might also derive this element from the non-oxidised sulphur of the food. In the absence of any decisive experiments in favour of either of these views, we must for the present leave this question unanswered.

The experiments of Laveran and Millon* have shown that it is only when taken in large doses that the alkaline sulphates are carried off in the stools, small doses being absorbed in the intestinal canal and eliminated by the kidneys. We should, however, be in error, if we assumed, as Laveran and Millon seem to do, that this salt is simply absorbed in the intestinal canal; for it is well known that, after the use of alkaline sulphates, there is an excessive development of intestinal gas, which is especially rich in sulphuretted hydrogen.

This conversion of the sulphates into sulphides in the intestine during digestion is further established by the following facts. If

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* Ann. d. Chim. et de Phys. T. 12, p. 13

I placed pure gluten, with milk-sugar and a little oil, in a dilute solution of sulphate of potash, and kept the mixture at a blood-heat, the mass first underwent the lactic fermentation, very soon became putrid, and, in the course of 6 or 8 days, unmistakeably developed sulphuretted hydrogen; in this way I was enabled, by the gradual addition of acetic acid, to remove the whole of the sulphuric acid from a mixture to which I had added 5 grammes of sulphate of potash. That the sulphate is, in like manner, deoxidised into the sulphide in the intestinal canal, where similar substances are brought in contact, is obvious from the composition of the stools which are discharged after the use of mineral waters, containing (like those of Marianbad) both sulphate of soda and carbonate of protoxide of iron.

In these fæces, which are usually green or black, I have recognised with certainty the presence of the sulphide of iron, but not of the bisulphide, as Kersten* seems to have done.

That the amount of sulphuric acid in the urine is chiefly due to the decomposition and oxidation of tissues containing sulphur is obvious from a comparison of the sulphates taken with the food and of those discharged by the urine.

As a mean of numerous experiments†, I found that the sulphates discharged with the urine amounted daily to 7·026 grammes, while I was living on an ordinary mixed diet. After a strictly animal diet for 12 days, the sulphates rose to 10·399 grammes; and, after the use of a strictly vegetable diet, they fell to 5·846 grammes. During these experiments I drank nothing to allay my thirst but common spring water, which, besides a little gypsum, contained only small quantities of alkaline sulphates; so that the striking difference in the amount of the excreted sulphates could not be traced to that head. Moreover, the extraordinary augmentation of the urea in the urine excreted during my animal diet indicated that this corresponding augmentation of the sulphates depended on the same cause, namely, on a decomposition and oxidation of the substances taken as food.

CARBONATE OF MAGNESIA.

This earthy salt occurs only sparingly in the animal organism. According to Berzelius‡, it is not improbable that the magnesia in the bones is combined with carbonic, and not with phosphoric acid, and that the phosphate of magnesia found in the bones is only formed during the analysis. This view is supported by the circumstance that carbonate of magnesia is found with carbonate and phosphate of lime in many pathological concretions. If, however, the magnesia were combined with carbonic acid in the bones, it should be taken up with the carbonate of lime by dilute acetic acid, and neither in my experiments nor in those of von Bibra has this been the case.

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* Journ. f. Chirurgie von Walther und Ammon. Bd. 2. S. 2.

† Journ. f. pr. Chem. Bd. 25, S. 2, and Bd. 27, S. 257.

‡ Lehrb. d. Chem. Bd. 9, S. 545.

Von Bibra* observes, in opposition to the view of Berzelius, that far more magnesia exists in the teeth than the carbonic acid found there can saturate.

Geiger† has published an analysis of a concretion extracted from the nose; it contained 76·7% of mineral substances, of which 8·3 were carbonate of magnesia. Bley‡ found 27·66% of carbonate of magnesia in a stony concretion from the peritoneum of a man.

A very large quantity of carbonate of magnesia exists in the urine of herbivorous animals, and hence we often meet with this salt in the urinary concretions of this class; it is very seldom found in human urinary calculi.

The urine of the ox, the camel, the horse, the rhinoceros, the elephant, the beaver, and the rabbit, deposites carbonate of magnesia with carbonate of lime. John§ found 10% of carbonate of magnesia in the mucous deposit of the urine of a horse suffering from diabetes.

Lassaigne‖ found 4·8% of this salt, with carbonate of lime, in a calculus from the bladder of an ox, while Wurzer¶ obtained 4·06%, and Wackenroder** 3·522% of carbonate of magnesia from calculi obtained from the horse. A calculus from the bladder of a man, which was analysed by Lindbergson††, contained, in addition to the phosphates of lime and magnesia, 2·55% of carbonate of magnesia, and only 3·14% of carbonate of lime. In two human calculi analysed by Bley‡‡, there were found 5·7% and 6·5% of carbonate of magnesia.

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* Op. cit. S. 94 and 287.

† Mag. f. Pharm. Bd. 21, S. 247.

‡ Arch. der Pharm. Bd. 20, S. 212.

§ Chem. Schriften. Bd. 6, S. 162.

‖ Journ. de Chim. méd. 2 Sér. T. 4, p. 49.

¶ Schweig. Journ. Bd. 8, S. 65.

** Ann. der Pharm. Bd. 18, S. 159.

†† Schweig. Journ. Bd. 32, S. 429.

‡‡ Buchner's Repert. 2. R. Bd. 2, S. 165.

It is worthy of remark that, while plants, and especially the grasses, contain almost all their magnesia in combination with phosphoric acid, the urine of herbivorous animals so frequently contains carbonate of magnesia. We can hardly suppose that the phosphate of magnesia in the animal body is robbed of its electro-negative constituent by a de-oxidation of the phosphoric acid, which is replaced by the weaker carbonic acid; it is much more probable that the combinations of lime with vegetable acids, conveyed into the animal body with the vegetable food, undergo such a decomposition with the phosphate of magnesia either in the blood or in other parts, that bone-earth and a vegetable salt of magnesia are formed, the latter being subsequently converted into carbonate of magnesia. The fact that the urine of herbivorous animals is poor in phosphates seems to confirm this view.

The egg-shell of birds contains not only carbonate of lime, but also carbonate of magnesia; both these salts are in part derived from the embryo during the incubation of the egg. (Prout[*] and Lassaigne[†].)

MANGANESE.

Minute quantities of this metal exist in the animal organism as elsewhere, in association with iron: manganese, however, seems to differ from iron in being devoid of influence on the metamorphosis of the animal tissues, for it appears in comparatively larger quantities in the excretions than in any of the fluids that take part in the vital functions. Like other heavy metals incidentally occurring in the organism, it is principally separated by the liver; hence it is found in comparatively large quantity in the bile.

Manganese has been found by Vauquelin[‡] in the hair, and by Bley[§], Wurzer[‖], and Bucholz[¶], in gall-stones and urinary calculi. Weidenbusch found 0·12% of proto-sesquioxide of manganese, and 0·23% of peroxide of iron in the ash of the bile, analysed by Rose's method.

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[*] Philosophical Transactions for 1822, p. 381.

[†] Journ. de Chim. méd. T. 10, p. 193.

[‡] Ann. de Chim. T. 58, p. 41.

[§] Op. cit.

[‖] Op. cit.

[¶] Op. cit.

ALUMINA.

This body never occurs in the animal organism; it has only been found in certain fossil bones into which it has undoubtedly entered by infiltration. Its absence in the animal organism is easily explained; any alumina conveyed into the intestinal canal enters into insoluble combination with organic substances, especially with the constituents of the bile, which cannot be resorbed.

After taking 3 grammes of basic sulphate of alumina within the space of 48 hours, I was unable to find a trace of alumina in the whole of the collected urine; it was, however, present in the ash of the solid excrements. The excrements were entirely devoid of odour for some days after I took this substance.

ARSENIC.

Devergie* and Orfila† believed that they had found arsenic in all animal bones, and hence that it should be regarded as an integral constituent of the animal organism. Subsequent investigations have, however, shown that there must have been some fallacy in the method of analysis pursued by these chemists, and that this view is altogether erroneous.

When positive experiments seemed to show that arsenic existed in the bones, chemists thought they had found an explanation of the apparent fact in the circumstance that phosphorus and arsenic are so frequently associated together; if the discovery of Walchner and Schafhäutl that the sediments of most chalybeate waters contain arsenic had been then known, this would doubtless have been regarded as strong additional proof of the presence of arsenic in the animal organism.

Arsenic acts in so noxious a manner on the animal organism, even in the smallest doses (as we see from experiments on animals), that nature actively eliminates this deleterious substance as rapidly as possible from the body.

Meurer‡ has made experiments on horses (animals which, as is well known, can bear large doses of arsenic), and von Bibra§ on rabbits, from whence it appears that most of the arsenic is carried off with the solid excrements. Both observers also found the poison in the urine in no inconsiderable quantity. Of the solid parts of the animal body, the excreting organs, namely the liver and kidneys, are those in which most arsenic is found; it has however also been detected in the heart, lungs, brain, and muscles. Some of these results are confirmed by the experiments of Duflos and Hirsch[*].

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* Ann. d'Hygiène publ. Oct. 1839, p. 482.

† Ibid. Juill. 1840, p. 163.

‡ Arch. d. Pharm. Bd. 26, S. 15.

§ Untersuch. über die Knochen u. s. w. S. 112.

Schnedermann and Knop[†] could detect no arsenic in the bones of a pig which had lived for three quarters of a year in the neighbourhood of the silver works at Andreasberg, where cattle and poultry do not thrive in consequence of the constant evolution of arsenical vapours.

COPPER AND LEAD.

Both these metals have been found in very minute quantity in the healthy body by Devergie,[‡] Lefortier,[§] Orfila,[‖] Dechamps,[¶] and Millon,[**] and were regarded by these chemists as integral constituents of all the soft parts, as well as of the blood; but it is only recently that any very decisive experiments on this subject have been instituted, and they, at all events, prove beyond a doubt that copper exists in the *blood* of some of the lower animals and in the *bile* of the ox and of man.

Millon believed that he had found them in the *blood*, but Melsens[††] has brought forward reasons, and even direct experiments against this view. Since, however, the presence of copper in the bile of man and the ox has been determined with certainty, the blood must give traces of this metal, even though they be almost inappreciable. Moreover, E. Harless[‡‡] has found copper in the blood, and more particularly in the liver, of some of the lower animals, namely, the *cephalopoda*, *ascidiæ*, and *mollusca*. This observer found copper in the liver of *Helix pomatia;* von Bibra found it in the liver of *cancer pagyurus*, *acanthias*, *zeus*, &c., and observed that it stood in an inverse ratio to the iron. Copper was originally found in the bile and in gall-stones by Bertozzi,[*] and subsequently by Heller,[†] Gorup-Besanez,[‡] Bramson,[§] and Orfila.[||] I have been equally unsuccessful in demonstrating the presence of copper either in the human liver, or in the liver of the frog; in the latter case my experiment was made on 250 livers; and I have also failed in obtaining any indication of copper or lead in the blood, although I followed Millon's instructions.

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[*] Das Arsenik, seine Erkennung u. s. w. 1842.

[†] Journ. f. prak. Ch. Bd. 36, S. 471.

[‡] Ann. d'Hygiène publ. Juill. 1840, p. 180.

[§] Ibid. p. 97.

[‖] Mémoires de l'Acad. de Méd. T. 8, p. 522.

[¶] Compt. rend. T. 27, p. 389.

[**] Journ. de Pharm. 3 Sér. T. 13, pp. 86-88, [also Compt. rend. T. 26, p. 41, and Ann. de Chim. et de Phys. 3 Sér. p. 372.—G. E. D.]

[††] Ann. de Chim. et de Phys. 3 Sér. T. 23, pp. 358-372.

[‡‡] Müller's Arch. 1847, S. 148-157.

There can be no doubt that the small quantities of copper which have been actually found in the fluids of the higher animals are only to be regarded as incidental constituents, while the experiments of Harless seem to indicate that in the lower animals the copper stands in an essential relation to the blood-corpuscles.

All the investigations which have hitherto been made, seem to indicate the liver as the organ in which deleterious substances, and especially those of a metallic nature, as, for instance, arsenic, lead, antimony, bismuth, &c., are accumulated, in order that they may be gradually eliminated with the bile. Hence, even if copper were constantly found in the blood or in the bile, it would afford no reason why we should regard this metal as an integral constituent of those fluids.

As copper has not only been found in many mineral waters, (as, for instance, by Will,[¶] Buchner,[**] Keller,[††] and Fischer,[‡‡]) but often in plants, and even in corn (Girardin,[§§]) there is no difficulty in accounting for its presence in small quantities in the organisms of the higher animals.

SALTS OF AMMONIA.

Although many high authorities believe that they have found these salts in various parts of the animal body, yet if we put out of the question their occurrence in the excreted fluids, we must regard it as almost undoubted that no salt of ammonia is produced in the animal organism or found in the living parts.

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[*] Ann. di Chirurg. Milan, 1845, p. 32.
[†] Arch. f. Chem. u. Mikroskop. Bd. 3, S. 228.
[‡] Unters. über Galle. Erlangen, 1848, S. 95.
[§] Zeitschr. f. rat. Med. Bd. 4, S. 193.
[||] Journ. de Chim. méd. 3 Sér. T. 3, p. 434.
[¶] Ann. d. Ch. u. Pharm. T. 55, p. 16.
[**] Jahrb. f. pr. Pharm. Bd. 15, S. 20-25.
[††] Journ. f. pr. Ch. Bd. 40, S. 442-447.
[‡‡] Arch. der Pharm. Bd. 52, S. 268.
[§§] Journ. de Chim. méd. 3 Sér. T. 2, pp. 443-445.

In the sweat, especially in that from the axillæ, the occurrence of ammonia is incontestible. In the urine it is assumed to exist in larger quantities than is actually the case. In the solid excrements which may be regarded as already in a state of decomposition, and which very soon develope ammonia when exposed to the atmosphere, Berzelius* believes that there is no carbonate of ammonia. Important as is the occurrence of ammonia in the vegetable juices for the renovation of the nitrogenous compounds, the animal organism appears to stand in little need of this substance. Indeed the process of decomposition by which the individual constituents of the organs are reduced to effete nitrogenous matter, by no means gives rise to the formation of ammonia, for in that case we should certainly find a far larger quantity of the salts of this alkali in the excretions. Urea is the principal nitrogenous product of decomposition which is formed within the body from the nitrogenous substances.

The blood, chyle, lymph, and milk, the fluids of the egg, and the secretions of the serous membranes either contain no ammonia or only extremely small quantities of it. In the pulmonary exhalation, on the other hand, small quantities of ammonia may always be recognised with great certainty.

Almost all histogenetic substances develope ammonia when treated with dilute acids or alkalies.

Observers have often believed that they had detected hydrochlorate of ammonia by the microscope after evaporating the alcoholic extract of animal fluids, when in reality, they saw the efflorescing forms of chloride of sodium, which, in the presence of certain organic matters (as, for instance, in the chyle) and especially when rapidly evaporated, separates in arborescent groups very similar to those of hydrochlorate of ammonia.

Lecanu and Denis failed in detecting any salts of ammonia in the blood; Marchand and Colberg were equally unsuccessful in reference to the lymph, and Schwartz, and Simon, in reference to the milk.

Even in the urine the quantity of ammonia is extremely small, as is shown by the following experiments. I allowed the greater quantity of water in the morning urine to freeze, and thus obtained a very concentrated, almost wine-red urine, in which we might assume that there was no decomposition of the constituents; when carefully treated with caustic potash, it yielded a precipitate which even after remaining for a long time in contact with the urine, contained no uric acid; if salts of ammonia were contained in the urine, urate of ammonia would have been precipitated; but there was no deposit of this salt till after the addition of hydrochlorate of ammonia. Scherer and Liebig* have also convinced themselves of the absence of ammonia in normal urine. Heintz found that the ordinary urinary sediments consist of urate of soda with a little urate of lime, and only traces of urate of ammonia.

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* Lehrb. der Chem. Bd. 9, S. 180.

Marchand† was the first who ascertained with certainty that ammonia was present in the pulmonary exhalation; by means of the colourless hæmatoxylin discovered by Erdmann‡ he could detect it in the air of each individual respiration; moreover, when we employ sulphuric acid for the removal or determination of the water in experiments on the respiration, it is always found to contain ammonia.

In certain diseased conditions of the system very considerable quantities of ammonia are often found in the blood as well as in the urine. Winter§ thought that the presence of ammonia in the blood explained the phenomena of typhus, but ammonia may be detected in the blood in all severe cases of acute disease, especially in variola and scarlatina; there is no more constancy in the presence of ammonia in the blood during typhus, than there is in the presence of the crystals of the triple phosphate in the excrements. It is by no means strange that in this state of the system the urine should contain ammonia; the urine is, however, richest in ammonia when it undergoes decomposition within the bladder, as in cases of inveterate vesical catarrh or diseases of the spinal cord.

HYDROCYANIC ACID.

This acid never occurs preformed in the animal organism; even in the most varied of the metamorphoses and decompositions which occur during disease, we never meet with either the free acid or a metallic cyanide. This is readily accounted for, when we recollect that hydrocyanic acid, cyanogen, and the metallic cyanides, are only produced from nitrogenous substances at a high degree of temperature. But in spite of this, certain physiological chemists have shown no unwillingness either to assume that hydrocyanic acid, either in conjugation or in combination, exists preformed in histogenetic substances, or to avail themselves of its formation in the explanation of various chemico-vital processes; in short, to make it take a part in the equations by which they pretend to explain the different stages in the metamorphosis of the animal tissues. We only mention it here inasmuch as it belongs to the bodies which are produced during the artificial decomposition of animal substances, such, for instance, as acetic, valerianic, and œnanthylic acids; we refer to the decomposition of hippuric acid by mere heat, and to the decomposition of histogenetic substances by bichromate of potash or binoxide of manganese and sulphuric acid.

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* Ann. d. Ch. u. Pharm. Bd. 50, S. 198.

† Journ. f. pr. Ch. Bd. 33, S. 148, and Bd. 44, S. 35.

‡ Ibid. Bd. 27, S. 193-208.

§ Ann. d. Ch. u. Pharm. Bd. 48, S. 329.

HYDROSULPHOCYANIC ACID.

This acid does not occur in a free state, but only as sulphocyanide of sodium [or potassium.] It was discovered by Treviranus in the *saliva*, and has as yet been found in no other fluid.

Treviranus named it hæmatic acid (*Blutsäure*); and, because he found that it formed blood-red solutions with the persalts of iron, he attributed the colour of the blood to sulphocyanide of iron.

For a very long time it has been disputed, whether the ingredient in the saliva, which gives rise to this red colour with the persalts of iron, is actually sulphocyanogen. There is scarcely any subject in the whole domain of zoo-chemistry in which so many experiments have been made with such contradictory results. We believe, however, that no one who repeats the experiments of Pettenkofer[*] can entertain a doubt regarding the presence of sulphocyanogen in the saliva. Pettenkofer especially directs attention to two tests which he discovered for hydrosulphocyanic acid. Solutions of the acetate and formate of peroxide of iron are perfectly decolorised on boiling with alkaline chlorides, while this treatment has no apparent effect on sulphocyanide of iron: further, it is known that the persalts of iron do not decompose ferridcyanide of potassium; but if we heat a solution of sulphocyanide of iron, hydrocyanic acid is developed, and there is a precipitate of Prussian blue. Pettenkofer applied this treatment to the alcoholic extract of the saliva, and thus ascertained the presence of sulphocyanogen. Other chemists had previously made use of a test that had been discovered for the sulphocyanides, namely, a mixture of two solutions of sulphate of protoxide of iron and sulphate of oxide of copper (when sub-sulphocyanide of copper is precipitated) with the view of detecting this substance in the saliva. The alcoholic extract of saliva is free from sulphuric acid (for the sulphates are insoluble in alcohol); hence Pettenkofer thought that he might make a quantitative determination of the sulphocyanogen in the saliva, by oxidising the alcoholic extract with chlorate of potash and hydrochloric acid, and precipitating the sulphuric acid that was formed by chloride of barium.

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[*] Buchn. Repert. 2 R. Bd. 41, S. 289-313.

Sulphocyanogen is almost always present in human saliva; it is, however, occasionally absent, without any apparent physiological or pathological reason. It appears to be wanting in the secretion during salivation from any cause; at least, I could never detect it during the ptyalism following the use of mercury or iodine, or occurring in the course of typhus or other diseases.

Sulphocyanogen occurs also in the saliva of the dog and the sheep; I have examined the saliva of four different horses without detecting any traces of it; Wright asserts, however, that it occurs in the saliva of that animal.

Considering the extremely small quantity in which it occurs, and that it is often absent without any apparent bad consequence, it seems hardly probable that the alkaline sulphocyanides take any definite part in the process of digestion.

I have noticed several healthy, vigorous young men, whose saliva contained no sulphocyanogen, and yet who enjoyed the best digestion.

It would be very easy to explain, by chemical formulæ, how sulphocyanogen might be formed from the histogenetic substances; but, unfortunately, we as yet possess no facts to confirm us in the establishment of any particular chemical equation; it is better, therefore, frankly to confess that we know absolutely nothing regarding the place or the mode in which sulphocyanogen is formed in the animal organism.

END OF THE FIRST VOLUME.